

AD _____

(Leave blank)

AWARD NUMBER: W81XWH-09-2-0018

TITLE: Optical Quality, Threshold Target Identification and
Military Target Task Performance after Advanced Keratorefractive
Surgery

PRINCIPAL INVESTIGATOR: Kraig S. Bower, MD, FACS

CONTRACTING ORGANIZATION: Henry M. Jackson foundation for the
Advancement of Military Medicine
Rockville, Maryland 20852

REPORT DATE: May 2010

TYPE OF REPORT: Annual

PREPARED FOR: U.S. Army Medical Research and Materiel Command
Fort Detrick, Maryland 21702-5012

DISTRIBUTION STATEMENT: (Check one)

- ☒ Approved for public release; distribution unlimited
- ☐ Distribution limited to U.S. Government agencies only;
report contains proprietary information

The views, opinions and/or findings contained in this report are those of the author(s) and should not be construed as an official Department of the Army position, policy or decision unless so designated by other documentation.

REPORT DOCUMENTATION PAGE				<i>Form Approved</i> OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing this collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to Department of Defense, Washington Headquarters Services, Directorate for Information Operations and Reports (0704-0188), 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any penalty for failing to comply with a collection of information if it does not display a currently valid OMB control number. PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.					
1. REPORT DATE (DD-MM-YYYY) 01 MAY 2010		2. REPORT TYPE ANNUAL		3. DATES COVERED (From - To) 1 MAY 2009 - 30 APR 2010	
Optical Quality, Threshold Target Identification and Military Target Task Performance after Advanced Keratorefractive Surgery				5a. CONTRACT NUMBER W81XWH-09-2-0018	
				5b. GRANT NUMBER	
				5c. PROGRAM ELEMENT NUMBER	
6. AUTHOR(S) Kraig S. Bower, MD, FACS Email: Kraig.Bower@amedd.army.mil				5d. PROJECT NUMBER	
				5e. TASK NUMBER	
				5f. WORK UNIT NUMBER	
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) Henry M. Jackson Foundation for the Advancement of Military Medicine Rockville, MD 20852				8. PERFORMING ORGANIZATION REPORT NUMBER	
9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES) USA MED RESEARCH ACQ ACTIVITY DIRECTOR 820 CHANDLER STREET FORT DETRICK, MD 21702-5014 USA MED RESEARCH ACQ ACTIVITY				10. SPONSOR/MONITOR'S ACRONYM(S) USAMRAA USAMRMC	
				11. SPONSOR/MONITOR'S REPORT NUMBER(S)	
12. DISTRIBUTION / AVAILABILITY STATEMENT Approved for public release; distribution unlimited					
13. SUPPLEMENTARY NOTES					
14. ABSTRACT The purpose of the present study is to investigate the effect of advanced refractive surgery on task performance in a military operational setting. In this prospective, randomized treatment trial we will enroll 224 nearsighted soldiers to undergo wavefront-guided (WFG) photorefractive keratectomy (PRK), WFG laser in situ keratomileusis (LASIK), wavefront optimized (WFO) PRK or WFO LASIK (56 in each group). Subjects will undergo extensive clinical and military visual performance testing pre- and post-operatively. Night Vision and Electronic Sensors Directorate (NVESD) performance prediction models (the Target Task Performance [TTP] metric) will analyze data derived from the contrast sensitivity function to predict whether there is a significant difference in either the range at which target identification can be made or the time a target can be detected. Military task performance will be further evaluated by the NVESD program (threshold target identification) in which tracked vehicle targets will be presented to observers at a sufficient distance to stress the eye response. The percentage of correctly identified stimuli will be plotted as a function of range to produce a psychometric function. Finally, night firing range performance will be determined before and after surgery. Study design will enable comparison to preoperative performance as well as comparisons between treatment groups.					
15. SUBJECT TERMS Military, Refractive Surgery, PRK, LASIK, Night Vision, Wavefront Optimized, Wavefront Guided, Visual Performance, Quality of Vision, Outcomes, Contrast Sensitivity					
16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			19b. TELEPHONE NUMBER (include area code)
U	U	U	SAR	130	

Table of Contents

	<u>Page</u>
Introduction.....	4
Body.....	4
Key Research Accomplishments.....	5
Reportable Outcomes.....	6
Conclusion.....	6
References.....	6
Supporting Data.....	7
Appendices.....	7

INTRODUCTION

Visual performance is critical for the successful execution of many military tasks including target detection and identification. Although refractive surgery offers substantial benefits on the battlefield when compared to glasses, surgically induced higher order optical aberrations (HOA) may affect quality of vision in terms of contrast sensitivity, glare, haloes, and reduced night vision. Because most military operations occur in low light/low contrast setting, any further degradation of vision as a result of refractive surgery can adversely impact military task performance. Wavefront optimized (WFO) and wavefront guided (WFG) surgery aim to minimize HOA improve postoperative quality of vision. The purpose of the present study is to investigate the utility of these advanced refractive surgery technologies in the military. In a prospective, randomized treatment trial we will enroll 224 nearsighted soldiers to WFG photorefractive keratectomy (PRK), WFG LASIK, WFO PRK or WFO LASIK (56 in each group). This collaboration between the Center for Refractive Surgery at Walter Reed Army Medical Center (WRAMC) and the US Army Night Vision and Electronic Sensors Directorate (NVESD) will evaluate refractive surgery results in terms of subjective visual performance, objective optical quality, performance prediction modeling, and military task performance. Human subjects will be seen only after approval by the WRAMC Department of Clinical Investigation and the USAMRMC Human Research Protection Office.

BODY

With the 2005 Base Realignment and Closure Act Walter Reed Army Medical Center and the National Naval Medical Center in Bethesda will merge and form a new Walter Reed National Military Medical Center (WRNMMC). Construction is under way for a renovated North Campus in Bethesda and a new South Campus at Ft. Belvoir. As part of that realignment the Ophthalmology Services at the respective centers will combine to form an integrated ophthalmology service responsible to staff both hospitals, beginning in 2011.

In preparation for the BRAC and the new integrated ophthalmology service, the principal investigator, along with the Walter Reed Center for Refractive Surgery Deputy for Refractive Research, determined that a modification of the planned project would serve to better facilitate the long term success of the planned research activities. This recommendation was staffed with senior Ophthalmology leaders in the National Capital Area and it was decided that rather than purchasing a new expensive AMO excimer laser system to perform WFG treatments at WRAMC, the existing AMO excimer laser at NNMC would be used to perform the WFG treatments. This required submission of the already-approved WRAMC human use protocol to the NNMC IRB. While initially optimistic that this could be done in a reasonable amount of time, we found that the NNMC IRB process delayed the ultimate approval to begin the study by over 9 months.

A summary of changes that came about as part of the additional review process by the Navy IRB as well as recommendations by the Human Research Protections Office (HRPO) at MRMC are summarized in **Table 1**.

We still believe this tactical decision is in the best long-term interest of the study, but are significantly behind the original timeline outlined in the grant proposal. Nevertheless, we are now enrolling and treating subjects and anticipate successful completion of Phase I of the study.

Table 1: Summary of protocol changes required by Navy and HRPO:

(1) Drop the thin cornea subgroup
(2) The surgical procedure (PRK vs. LASIK) will no longer be randomized but rather the patient and the surgeon determine the preferred treatment plan. After that decision is made, the treatment type (WFG vs. WFO) and therefore location of the surgery (WRAMC vs. NNMC) is randomly assigned
(3) The study will be conducted in three phases
Phase 1 (112 patients) - no additional NVESD testing,
Phase 2 (56 patients) - NVESD target detection testing,
Phase 3 (56 patients) - night firing range

A copy of the full protocol, appropriate modifications, currently approved consent forms, and approval letters are attached as **Appendix 1** at the conclusion of this report.

As of the date of this report we have enrolled 24 patients, and treated 12 patients (5 WFG PRK, 1 WFG LASIK, 5 WFO PRK, and 1 WFO LASIK). Twelve patients are currently awaiting final pre-op testing and surgery. There have been no complications as a result of the study surgeries and no subject has disenrolled from the study.

KEY RESEARCH ACCOMPLISHMENTS

- Initial WRAMC Department of Clinical Investigation approval (11/7/2008)
- Initial NNMC IRB approval, PI is LCDR David Cute (10/21/2009)
- NNMC approval of HRPO required modifications (1/12/2010)
- WRAMC DCI approval of NNMC and HRPO modifications (2/17/2010)
- HRPO approval (2/27/2010)
- MOU between WRAMC-NVESD-NNMC completed (3/12/2010)

- CRADA between WRAMC-NVESD awaiting final signature at NVESD
- Cambridge system – worked out bugs and got testing protocol down to approximately 20 minutes and reconfigured study lane for contrast testing. Training of key CRS research personnel on administration of the examination.
- Meeting with NVESD’s Brad Preece to verify initial Cambridge results and suitability of data for NVESD modeling (6/1/2010)
- Obtained AMO Wavescan for pre-op registration of wavefront aberrometry for WFG treatments. Training of technicians on AMO Wavescan; total of 4 sessions with AMO rep, concentrating on registration of aberrometry measurements for use in WFG surgery. Also engaged in training of WRAMC surgeons in interpretation and selection of best scan for use in treatments.
- Obtained and installed COAS-HD wavefront aberrometer for wavefront measurements (3/1/2010). Due to problems with the acquisition head the unit was returned to the manufacturer for trouble-shooting and repair. The new unit was returned to the CRS 6/1/2010 and is fully operational.
- Briefing and training of all CRS staff on the protocol-background, study design, responsibilities of all CRS staff including research personnel, front desk, technicians, and optometrists. Appropriate handout material and flow diagrams given and posted in CRS common areas for reference.
- Began screening patients for study enrollment (3/19/2010). Enrolled and completed clinical preoperative evaluations on first patients.
- Performed first WFO study treatments at WRAMC (4/26/2010) and first WFG study treatments at NNMC (4/29/2010).
- Submitted no-cost extension request to HMJ.
- Initiated budget reprogramming request at HMJ.

REPORTABLE OUTCOMES

None

CONCLUSION

None

REFERENCES

None

SUPPORTING DATA

None

APPENDICES

Full IRB protocol, consent forms, and approval letters.



DEPARTMENT OF THE ARMY
US ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
504 SCOTT STREET
FORT DETRICK, MD 21702-5012

REPLY TO
ATTENTION OF

MCMR-RP

27 February 2010

MEMORANDUM FOR THE RECORD

SUBJECT: Initial Approval for the Protocol, "Optical Quality, Threshold Target Identification, and Military Target Task Performance After Advanced Keratorefractive Surgery," Submitted by COL Kraig S. Bower, MC, Henry M. Jackson Foundation for the Advancement of Military Medicine, Rockville, Maryland, Proposal Log Number PR080107, Award Number W81XWH-09-2-0018, HRPO Log Number A-15426

1. The subject protocol was approved by the Walter Reed Army Medical Center (WRAMC) Human Use Committee (HUC) on 12 February 2010 and by the National Naval Medical Center (NNMC) on 12 January 2010. This protocol was reviewed by the U.S. Army Medical Research and Materiel Command (USAMRMC), Office of Research Protections (ORP), Human Research Protection Office (HRPO) and found to comply with applicable Federal, DOD, U.S. Army, and USAMRMC human subjects protection requirements.
2. This no greater than minimal risk study is approved for the enrollment of 224 subjects.
3. Please note the following reporting obligations:
 - a. Major modifications to the research protocol (including the later phase of the work to be performed at the Night Vision and Electronic Sensors Directorate) and any modifications that could potentially increase risk to subjects must be submitted to the USAMRMC ORP HRPO for approval prior to implementation. All other amendments must be submitted with the continuing review report to the HRPO for acceptance.
 - b. All unanticipated problems involving risks to subjects or others, serious adverse events related to study participation, and deaths related to study participation must be reported promptly to the HRPO.
 - c. Any deviation to the subject protocol that affects the safety or rights of the subject and/or integrity of the study data must be reported promptly to the HRPO.
 - d. All modifications, deviations, unanticipated problems, adverse events, and deaths must also be reported at the time of continuing review of the protocol.

MCMR-RP

SUBJECT: Initial Approval for the Protocol, "Optical Quality, Threshold Target Identification, and Military Target Task Performance After Advanced Keratorefractive Surgery," Submitted by COL Kraig S. Bower, MC, Henry M. Jackson Foundation for the Advancement of Military Medicine, Rockville, Maryland, Proposal Log Number PR080107, Award Number W81XWH-09-2-0018, HRPO Log Number A-15426

e. A copy of the continuing review report approved by the WRAMC HUC and the continuing review report approved by the NNMC must be submitted to the HRPO as soon as possible after receipt of approvals. It appears the next continuing review is due by the WRAMC HUC no later than 11 August 2010 and by the NNMC no later than 9 July 2010.

f. In addition, the current version of the protocol and consent form (if applicable) must be submitted along with the continuing review report and the approval notices from both the WRAMC HUC and the NNMC for continuation of the protocol.

g. The final study report submitted to the WRAMC HUC and the NNMC, including a copy of any acknowledgement documentation and any supporting documents, must be submitted to the HRPO as soon as all documents become available.

4. Do not construe this correspondence as approval for any contract funding. Only the Contracting Officer or Grants Officer can authorize expenditure of funds. It is recommended that you contact the appropriate contract specialist or contracting officer regarding the expenditure of funds for your project.

5. The HRPO point of contact for this study is Johanna Kidwell, BS, Human Subjects Protection Scientist, at 301-619-7486/Johanna.Kidwell@us.army.mil.

ANDREA J. KLINE, MS, CIP
Chief, Research Administrative Support
Human Research Protection Office
Office of Research Protections



DEPARTMENT OF THE ARMY
WALTER REED ARMY MEDICAL CENTER
WALTER REED HEALTH CARE SYSTEM
WASHINGTON, DC 20307-5001

REPLY TO
ATTENTION OF

MCHL-CI

DATE: February 17, 2010

TO: Kraig S. Bower, MD
FROM: Dr. Sarathy Komanduri, Asst. Chief, Research Review Services

STUDY TITLE: [20481-3] Optical Quality, Threshold Target Identification, and Military Target Task Performance after Advanced Keratorefractive Surgery

REFERENCE #: 08-6967(2)

SUBMISSION TYPE: Amendment/Modification

ACTION: APPROVED

APPROVAL DATE: February 12, 2010

EXPIRATION DATE: August 11, 2010

REVIEW TYPE: Full Committee Review

1. Your memorandum was received by DCI on 19 Jan 2010 and was reviewed and approved by the WRAMC Human Use Committee (HUC) on February 12, 2010

- with no revisions.

You may incorporate the changes indicated by this addendum upon receipt of this letter.

- No HIPAA changes were submitted in this addendum.
- **Enclosed are the approved revised consent form(s) that must be duplicated and used for enrolling the subjects.** Also uploaded is the exact duplicate of the consent form in Word version in case you should need it in the future.

2. If your study has been approved for acceptance of loaned equipment or the provision of an (IND) drug/ Placebo, (IDE) device, supplies and/or gift or money or property, you must coordinate this requirement with [Ms. Word], Research Administration Service, DCI, Building #6, Room 4009 at [782-7859]. Only Pharmacy Service, not the principal investigator, is authorized to receive and dispense drugs.

3. The protocol was originally approved on August 12, 2008.

4. If you have any questions, please contact Kristin Beltz at 202 782-7848.

Asst. Chief, Research Review Service

Department of Clinical Investigation

"Electronic Signature Notice: In accordance with the "Government Paperwork Elimination Act" (GPEA) (Pub.L. 105-277; codified at 44 USC 3504); Federal and DOD applicable instructions, directives and regulations, documents have been electronically signed and authorized by all who have been required to do so. These signatures have the same effect as their paper-based counterparts. Verification is retained within our protected electronic records and audit trails."



DEPARTMENT OF THE NAVY

NATIONAL NAVAL MEDICAL CENTER
BETHESDA, MARYLAND 20889-5600

IN REPLY REFER TO

6500
14IV00/053

12 JAN 2010

From: Commander, National Naval Medical Center
To: LTC C. Coe, MC, USA

Subj: APPROVAL OF AMENDMENT #1 (MODIFIED PROTOCOL AND REVISED CONSENT FORM) FOR RESEARCH PROJECT NNMCMC.2009.0051, "OPTICAL QUALITY, THRESHOLD TARGET IDENTIFICATION, AND MILITARY TARGET TASK PERFORMANCE AFTER ADVANCED KERATOREFRACTIVE SURGERY"

Ref: (a) Your email message of 5 Nov 09 w/attachments
(b) RCRS/IRB memo 6500 Ser 14IV00/101 of 23 Nov 09
(c) SECNAVINST 3900.39D

Encl: (1) Revised Consent Form


1. Per reference (a), amendment #1, (modified the protocol and revised consent form), has been reviewed and recommended for approval, reference (b), using reference (c), and is approved. These changes to research project NNMCMC.2009.0051 will be documented in the 14 January 2010 IRB meeting minutes.

3. Enclosure (1) is the stamped IRB approved consent form. Enclosure (1) is to be duplicated and used to enroll subjects. Keep the signed, original consent form and HIPAA form in your project file; give each subject a copy of their signed documents; and place a copy of the signed documents in each subject's medical record.

4. You are reminded that this research protocol has not yet received approval letter from NNMCMC, Commander pending an implemented Memorandum of Understanding (MOU) between National Naval Medical Center (NNMCMC) and Fort Belvoir Army Medical Center (FBAMC) and Walter Reed Army Medical Center (WRAMC).

5. Be sure to maintain complete records concerning these changes with your original project file.

6. Please do not hesitate to contact the Responsible Conduct of Research Service (RCRS) staff at (301) 295-2275 for any assistance or concerns.


T. D. GLEESON
By direction

Copy to:
Research Coordinator
Study File
BUMED, HRPP
NNMCMC.2009.0051.AM1.EP9.A

1A

**Department of Defense
Human Research Protection Program**

**DOD INSTITUTIONAL AGREEMENT
FOR INSTITUTIONAL REVIEW BOARD (IRB) REVIEW
BETWEEN**

**National Naval Medical Center (NNMC)
Bethesda, Maryland**

AND

**Walter Reed Army Medical Center (WRAMC)
Washington, D.C.**

**Part 1
INSTITUTION INFORMATION**

This DoD Institutional Agreement for IRB Review describes the responsibilities of the institutions engaged in the research involving human subjects. This Agreement, when signed, becomes part of each institution's Federal Assurance for the Protection of Human Research Subjects (e.g., DoD Assurance for the Protection of Human Research Subjects or Department of Health and Human Services (DHHS) Federalwide Assurance (FWA)).

A. Institutions Relying on the IRBs:

Name: National Naval Medical Center (NNMC)
DoD Assurance Number: DoD-N 40001
DHHS FWA Number: FWA00000366

Name: Walter Reed Army Medical Center (WRAMC)
DoD Assurance Number: DoD-A 10013
DHHS FWA Number: FWA00000477
DHHS IRB Number: IRB00000662

B. Institutions Supplying IRB Services:

Name: Walter Reed Army Medical Center (WRAMC)

C. Scope:

This Agreement applies to: All research performed by the institutions, on a case-by-case basis. Determination of the reviewing IRB is to be based on location of the subject/patient population, funding, Principal Investigator's affiliation, and other decisional factors, and is

to be made by both NNMC and WRAMC collaboratively. If there is a difference of opinion regarding this determination, the Department Head of Responsible Conduct of Research Service, NNMC and Director, of Clinical Investigations Department, WRAMC are responsible for coming to an agreement as to which IRB should review a particular study, or elect to have both IRBs review.

D. Effective Dates:

This Agreement is effective as of the date approved and signed by the DoD Component Designated Official and expires on the date listed in the approval document.

Part 2
INSTITUTIONAL RESPONSIBILITIES

All institutions are responsible for ensuring that their personnel (i.e., the Institutional Official, the IRB, IRB office staff, investigators and research staff, and any other personnel supporting research covered under this Agreement) act in accordance with all applicable federal, state and local laws and regulations (e.g., Title 32 Code of Federal Regulations Part 219 (32 CFR 219; Title 10 United States Code Section 980 (10 USC 980); DoD Directives and Instructions (e.g., DoDD 3216.02); AR 40-38, 45 CFR Part 46 (Subparts B, C, and D as made applicable by DoDD 3216.02); DoD Component policies; and the Food and Drug Administration policies (e.g., 21 CFR Parts 50, 56, 312, and 812) where applicable in addition to the terms and conditions of the organizations' DoD Assurance and/or their DHHS FWA.

Specific DoD Component requirements are stated in Part 3 of this document.

All institutions will permit, upon request, the inspection of any facilities used in support of the activities described in the "Scope" and other research areas by federal agencies responsible for oversight of human research protection and proper management of the research within the scope of this agreement.

A. The Institutional Official of the Engaged Institutions will:

1. Ensure that all institutional personnel involved in the research (covered within the scope of this agreement) have completed education and training requirements.
2. Verify that scientific review of the research protocol has been conducted and that the IRB considered the feedback from the scientific review.
3. Verify that the IRB has reviewed the research protocol in accordance with DoD requirements, including those identified in the research contract or agreement.
4. Ensure institutional personnel comply with requirements and oversight established by the IRB.
5. Ensure institutional personnel follow the approved research protocol.

6. Ensure institutional personnel report to the IRB and DoD: (a) unanticipated problems involving risks to subjects or others, (b) serious or continuing non-compliance, (c) suspension or termination of IRB approval, and (d) any other events or circumstances requiring notification.

7. Ensure institutional personnel maintain current copies of the IRB approved research protocol (initial review, continuing review, amendments, adverse event reports, and final report), all communications with the IRB, this Agreement, and other relevant information in accordance with DoD record keeping requirements.

8. Verify the IRB has the expertise and policies and procedures needed to review and oversee the research submitted by the institution (in accordance with 32 CFR 219.107, §.103(b)(3), and §.115).

B. The Institutions Supplying the Reviewing IRB will:

1. Verify that personnel involved in the research have completed required education and training for the protection of human research subjects.

2. Verify that the IRB is properly constituted for reviewing the study

3. Fulfill the IRB responsibilities identified in the engaged institution's Assurance.

4. Provide IO of the engaged institution with information about the IRB, such as a list of IRB members or expertise and the written procedures for executing IRB responsibilities in accordance with paragraph A.8 above.

5. Provide to the engaged institution conducting the research and the Principal Investigator(s) a copy of the IRB's review and determinations concerning the research.

6. Provide relevant sections of the IRB meeting minutes to the engaged institution.

7. Maintain current copies of the IRB approved research protocol (initial review, continuing review, amendments, adverse events reports, and final report), all communications with the institution, this Agreement, and other relevant information in accordance with DoD Component record-keeping requirements.

C. Amendments and Termination:

1. This Agreement may be modified, cancelled, or renegotiated upon mutual consent, at any time through an amendment signed by authorized representatives of the organizations, the Commander, NNMCC and the Commanding Officer, WRAMC. A decision to amend or terminate will be submitted to the DoD Component Designated Official.

2. The DoD Component Designated Official is not obligated to approve this Agreement.

Part 3
DOD COMPONENT REQUIREMENTS

A. The Institutions will comply with the requirements of the DoD Component issuing this Agreement. These requirements are identified in Part 3, paragraph B. DoD Components may require that other research, not specifically identified by 32 CFR 219, also comply with the terms of this Agreement (32 CFR 219.101(d)).

B. When the Institutions conduct research supported by or in collaboration with an organization of another DoD Component, this Institution must comply with the policies and procedures of that organization. The requirements of the collaborating DoD Components are identified below:

Department of the Army

AR 70-25 Use of Volunteers as Subjects of Research, 25 January 1990;
AR 40-38, Clinical Investigation Program, 1 September 1989;
AR 40-7, Use of Investigational Drugs in Humans and the Use of Schedule I Controlled
Drug Substances, 4 January 1991

Department of the Navy

SECNAVINST 3900.39D of 6 November 2006

Part 4
INSTITUTIONAL AGREEMENT

A. Engaged Institution Relying on the External IRB

1. NNMCI Institutional Signatory Official

Acting in an authorized capacity on behalf of this Institution and with an understanding of the Institution's responsibilities under its Assurance, I assure protections for human subjects as specified above.

Signature:



Name: Matthew L. Nathan

Rank/Grade: RDML, MC, USN

Institutional Title: Commander

Mailing Address: 8901 Wisconsin Ave

Building 10

Bethesda, MD 20889

Email address: Matthew.Nathan@med.navy.mil

Date: 1-5-09

Telephone number: 301-295-5800

FAX number: 301-295-1480

2. NNMCI IRB Chair Agreement:

Acting in an authorized capacity on behalf of the IRB and with an understanding of the Institution's responsibilities under this Assurance, I assure protections for human subjects as specified above.

Signature:



Name: Timothy F. Donahue

Rank/Grade: CDR, MC, USN

Institutional Title: National Naval Medical Center

Mailing Address: 8901 Wisconsin Ave

Building 10

Bethesda, MD 20889

Email address: Timothy.F.Donahue@med.navy.mil

Date: 12-11-08

Telephone number: 301-295-4262

FAX number: 301-295-1490

3. Human Research Protection Primary Contact for the NNMCI DoD IRB

Name: Jeffrey T. Lenert

Rank/Grade: CAPT, MC, USN

Institutional Title: Head, Responsible Conduct of Research Service

Mailing Address: 8901 Wisconsin Avenue

Bldg. 1, 4th Floor, Room 4394

Bethesda, MD 20889

Email address: Jeffrey.Lenert@med.navy.mil

Telephone number: 301-295-2275

FAX number: 301-295-1490

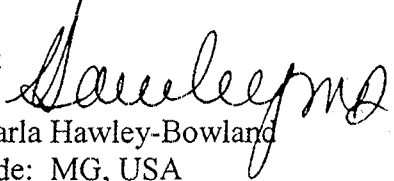
Part 4
INSTITUTIONAL AGREEMENT

B. Engaged Institution with the IRB-WRAMC

1. Institutional Signatory Official:

Acting in an authorized capacity on behalf of this Institution and with an understanding of the Institution's responsibilities under its Assurance, I assure protections for human subjects as specified above.

Signature:



Date: 08/11/09

Name: Carla Hawley-Bowland

Telephone number: 202-782-1104

Rank/Grade: MG, USA

FAX number: 202-782-0940

Institutional Title: Commanding, NARMC

Mailing Address: Bldg 1, Command Suite,
6900, Georgia Avenue, NW
Washington, DC 20307-5001

Email address: Carla.Howley-Bowland@us.army.mil

2. IRB Chair Agreement:

Acting in an authorized capacity on behalf of the IRB and with an understanding of the Institution's responsibilities under this Assurance, I assure protections for human subjects as specified above.

Signature:



Date:

Name: Dr. Robert Dean, MC

Telephone number: 202-782-7128

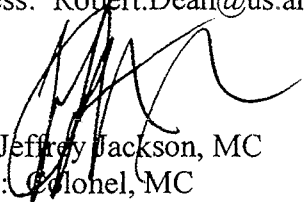
Rank/Grade: Colonel, MC

Institutional Title: Walter Reed Army Medical Center

Mailing Address: 6900, Georgia Avenue, NW
Washington, DC 20307-5001

Email address: Robert.Dean@us.army.mil

Signature:



Date: 28 Oct 08

Name: Dr. Jeffrey Jackson, MC

Telephone Number: 202-782-5603

Rank/Grade: Colonel, MC

Institutional Title: Walter Reed Army Medical Center

Mailing Address: 6900, Georgia Avenue, NW
Washington, DC 20307-5001

Email address: Jeffrey.L.Jackson@us.army.mil

3. Human Research Protection Primary Contact:

Name: Charles E. McQueen Telephone Number: 301-319-4176
Rank/Grade: Colonel, MC
Institutional Title: JTF CapMed; J7 Chief of Research
Mailing Address: 8901 Wisconsin Ave, Bethesda, MD 20889
Telephone Number: 301-319-4176
Email Address: Charles.McQueen@med.navy.mil

MEMORANDUM OF UNDERSTANDING

BETWEEN

**WALTER REED ARMY MEDICAL CENTER (WRAMC)
WASHINGTON, D C**

AND

**NIGHT VISION ELECTRONIC SENSORS DIRECTORATE (NVESD)
FT BELVOIR, VIRGINIA**

AND

**NATIONAL NAVAL MEDICAL CENTER,
BETHESDA, MARYLAND**

I. GENERAL

A. The National Naval Medical Center, Bethesda, Maryland, herein referred to as NNMC, has established this agreement for the purpose of conducting clinical investigation research in support of education and patient care. This program requires collaboration with Walter Reed Army Medical Center (WRAMC), Washington, DC, and Night Vision Electronic Sensors Directorate (NVESD), Ft. Belvoir, Virginia.

B. It is mutually beneficial to NNMC, WRAMC and NVESD to allow physicians and other health care providers and scientists to participate in research to enhance the quality of patient care and to contribute to staff education and training. This new agreement is in support of a Responsible Conduct of Research Department Project #NNMC.2009.0051, "Optical Quality, Threshold Target Identification, and Military Target Task Performance after Advanced Keratorefractive Surgery." LTC Charles Coe, MC, USA, is the Deputy & Research Director, Center for Refractive Surgery at WRAMC and involved with the research. The WRAMC Principal Investigator is COL Kraig S. Bower, MC, USA. The NNMC Principal Investigator is CDR David L. Cute, MC, USN. Mr. Brian S. Miller is the primary contact person at NVESD.

C. The purpose of this research collaboration is to compare wavefront guided (WFG) versus wavefront optimized (WFO) keratorefractive surgery. This collaborative effort will be broken down into 4 main tasks.

Task 1: Screen and enroll patients, perform preoperative clinical exam, perform pre-operative visual function testing at WRAMC (Research Months 1-36)

- Begin screening and enrolling 224 subjects at WRAMC
- Perform pre-operative cycloplegic refraction and ocular health examinations on all 224 subjects at WRAMC (Research Months 1-24)
- Measure all 224 subjects' contrast sensitivity function at WRAMC (Research Months 1-24)
- Measure all 224 subjects' wavefront aberration map at WRAMC (Research Months 1-24)

• **Task 2:** Performance of advanced keratorefractive surgery (in Research Months 1-24)

- Perform WFG refractive surgery using the VISX STAR S4 on 112 subjects. Fifty-six (56) subjects will undergo WFG Intralase LASIK, and 56 subjects will undergo WFG photorefractive keratectomy (PRK). All WFG surgeries will be performed at NNMC.

MEMORANDUM OF UNDERSTANDING BETWEEN THE NATIONAL NAVAL MEDICAL CENTER, BETHESDA, MARYLAND, WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC AND NIGHT VISION ELECTRONIC SENSORS DIRECTORATE, FT. BELVOIR, VIRGINIA

Surgical procedures will be randomized between CDR Cute and COL Bower with each surgeon performing surgery on approximately 56 patients. (Research Months 1-24)

- Perform WFO refractive surgery using the ALLEGRETTO WAVELIGHT Wave Eye-Q on 112 subjects. Fifty-six (56) subjects will undergo WFO Intralase LASIK, and 56 subjects will undergo WFO PRK. All WFO surgeries will be performed at WRAMC. Surgical procedures will be randomized between CDR Cute and COL Bower with each surgeon performing surgery on approximately 56 subjects. (Research Months 1-24)

Task 3: Develop, test, and validate military metrics of visual performance that measure a human observer's ability to detect and discriminate objects of interest within a static or a dynamic sequence of images. The testing involved in this task will be performed at the NVESD, in Research Months 1-36. The following testing will be done:

- Visual performance prediction modeling. All 224 subjects will be tested and put into 4 groups (56 subjects per group): WFG PRK, WFG LASIK, WFO PRK, and WFO LASIK. Utilize objective target acquisition metrics to predict visual performance by measuring the subjects' contrast sensitivity function (which was done at WRAMC) and comparing it to the NVESD target task performance (TTP) metrics. There will also be a comparison of pre- and post surgical results in research months 2-36.
- Psychophysical measurement of threshold target identification and detection. Fifty-six (56) subjects will be tested (14 per group, in 4 groups): WFG PRK, WFG LASIK, WFO PRK, and WFO LASIK. *Target identification* will be tested with a 12 alternative forced choice paradigm. The percentage of correctly identified stimuli will then be plotted as a function of range to produce a psychometric function. Outcome measures of threshold target identification at certain ranges/distances will be compared pre-operatively, at 6 weeks post-operatively, and at 6 months post-operatively. *Target detection* involves searching and detecting vehicle targets in a cluttered environment. The probability of target detection will then be plotted as a function of time to produce a psychometric function. Outcome measures involve the average time required to detect threshold targets and will be compared pre-operatively, at 6 weeks post-operatively, and at 6 months post-operatively. This will be done in research months 6-30.
- Weapons (M16A3) performance. Fifty-six (56) subjects (14 per group, in 4 groups) will be tested: WFG PRK, WFG LASIK, WFO PRK, WFO LASIK. They will be at a rifle range in mesopic conditions. Performance will be scored pre-operatively, at 6 weeks post-operatively, and at 6 months post-surgery. Outcome measure will be accuracy (average distance from target center) and precision (standard deviation of distance to target). Comparison will be made pre- and post- surgery. Testing will be done in research months 6-30.

Task 4: Determine efficacy of WFG ablations (PRK and LASIK) versus WFO ablations (PRK and LASIK), and determine efficacy of refractive surgery methods (PRK versus LASIK). This will be done in research months 30 to 36. This task will be done by COL Bower.

- Conduct 1-, 3-, 6-and 12-month post-operative evaluations, cycloplegic refractions, contrast sensitivity testing, and measurement of wavefront map/monochromatic optical aberrations on all 224 subjects at WRAMC. This will be done in research months 6-30.

MEMORANDUM OF UNDERSTANDING BETWEEN THE NATIONAL NAVAL MEDICAL CENTER, BETHESDA, MARYLAND, WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC AND NIGHT VISION ELECTRONIC SENSORS DIRECTORATE, FT. BELVOIR, VIRGINIA

- Comparison of pre-operative objective measures of optical quality to post-operative values and comparison of pre-operative to postoperative cycloplegic refraction on all 224 subjects at WRAMC in research months 30-36.
- Determine efficacy of ablation pattern (WFG v. WFO) on outcome variables at WRAMC in research months 30-36.
- Compare efficacy of refractive surgery method (PRK v. LASIK) on all 224 subjects at WRAMC in research months 30 to 36.
- Utilize a 2x2 factorial design (WFG PRK, WFG LASIK, WFO PRK, WFO LASIK) and 2 Way-ANOVA to determine if either a main or interaction effect exist between the two independent variables (Surgical Procedure (PRK v. LASIK) and Ablation Profile (WFG v. WFO) at WRAMC in research months 30 to 36 on all 224 subjects.

D. This protocol is a federally funded project. NVESD received a federal grant of \$88,000.00 in federal funds to perform the specific psychophysical testing and data analysis as part of this research project. NVESD has also provided a letter of support for testing and data analysis services.

II. UNDERSTANDING

A. Insofar as the Commander, NNMC deems it appropriate and consonant with this command's basic mission, NNMC will:

1. Provide that all research to be conducted at the NNMC will be reviewed and approved in accordance with applicable NNMC, Office of Research Integrity & Ethics (ORI&E), Chief, Bureau of Medicine and Surgery, Secretary of the Navy, and Department of Defense (DOD), and Federal Drug Administration (FDA) instructions and regulations.
2. Ensure the privileges, and as applicable, verify the license, of those physicians and other health care providers and scientists, who would be participating in research.
3. Provide training for NNMC personnel in protocol requirements to ensure adherence with the study protocols, data quality, and completeness of reporting for the research project.
4. Agree that all data accrued/generated through this research project become the property of the Departments of the Army (DOA) and the Navy (DON), respectively. Upon execution of this Memorandum of Understanding (MOU), research data will be exchanged between the participating institutions.
5. Through direction of the investigators, share authorship, as appropriate and agreed upon, on any publications or presentations derived from this research. NNMC will use established procedures for the clearance of all NNMC investigator publications and presentations resulting from the Research Project. Any materials compiled or published by NNMC staff must clearly contain (i) all appropriate DOD/DOA/DON disclosures and disclaimers stating that opinions or assertions contained herein are those of the writer and are not to be construed

MEMORANDUM OF UNDERSTANDING BETWEEN THE NATIONAL NAVAL MEDICAL CENTER, BETHESDA, MARYLAND, WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC AND NIGHT VISION ELECTRONIC SENSORS DIRECTORATE, FT. BELVOIR, VIRGINIA

as official or reflecting the views and opinions of the DOD/DOA; (ii) a statement of ethical Institutional Review Board (IRB) approval of research involving human subjects; (iii) acknowledgement of DOD/DOA/DON or other support; (iv) a security and policy review; and (v) certification that all authors were listed and identified on the publication.

6. Permit, upon request, the inspection of appropriate clinical facilities and other research areas by agencies charged with the responsibility for the accreditation of the institution and proper management of the Research Project.
7. Perform WFG (PRK and LASIK surgery) and assist, as needed, in the screening and enrollment of subjects, performance of pre-operative clinical examinations, performance of pre-operative visual function testing, and collaboration of the analysis of data to determine efficacies identified in Task 4.

B. The WRAMC will:

1. Provide that all research to be conducted at the WRAMC will be reviewed and approved in accordance with applicable WRAMC, DOA, and DOD instructions and regulations.
2. Ensure the privileges, and as applicable, verify the license, of those physicians and other health care providers and scientists, who would be participating in research.
3. Provide training for WRAMC personnel in protocol requirements to ensure adherence with the study protocols, data quality, and completeness of reporting for the research project.
4. Agree that all data accrued/generated through this research project become the property of the DOA and the DON, respectively. Upon execution of this MOU, research data will be exchanged between the participating institutions.
5. Through direction of the investigators, share authorship, as appropriate and agreed upon, on any publications or presentations derived from this research. WRAMC will use established procedures for the clearance of all WRAMC investigator publications and presentations resulting from the Research Project. Any materials compiled or published by WRAMC staff must clearly contain (i) all appropriate DOD/DOA/DON disclosures and disclaimers stating that opinions or assertions contained herein are those of the writer and are not to be construed as official or reflecting the views and opinions of the DOD/DOA; (ii) a statement of ethical IRB approval of research involving human subjects; (iii) acknowledgement of DOD/DOA/DON or other support; (iv) a security and policy review; and (v) certification that all authors were listed and identified on the publication.
6. Permit, upon request, the inspection of appropriate clinical facilities and other research areas by agencies charged with the responsibility for the accreditation of the institution and proper management of the Research Project.

MEMORANDUM OF UNDERSTANDING BETWEEN THE NATIONAL NAVAL MEDICAL CENTER, BETHESDA, MARYLAND, WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC AND NIGHT VISION ELECTRONIC SENSORS DIRECTORATE, FT. BELVOIR, VIRGINIA

7. Screen and enroll subjects, perform pre-operative clinical examinations, perform pre-operative visual function testing, perform WFO (PRK and LASIK) surgery, and analyze data to determine efficacies identified in Task 4.

C. The NVESD will:

1. Provide the names of the individuals who will participate in the Research Project.
2. Provide that all testing to be conducted at NVESD will be reviewed and approved in accordance applicable regulations and pursuant to the federal grant.
3. Share authorship, as appropriate and agreed upon, on any publications or presentations derived from this research.
4. Permit, upon request, the inspection of appropriate research areas by agencies charged with responsibility for the proper management of the Research Project.

III. TECHNICAL INFORMATION

A. Information. Each party acknowledges that it may disclose certain information to the other party in furtherance of this research study, and it may contain proprietary data. If any party discloses such proprietary data to another party, the disclosing party will designate such information as proprietary by clear identification and marking, and the receiving party will:

1. Use at least the same degree of care to maintain the secrecy of such proprietary information as such party uses to maintain the secrecy of its own proprietary information.
2. Use the proprietary information only in connection with the Research Project and to otherwise accomplish the purpose of this Agreement.

B. Disclosure. Each party may disclose such information to its employees, representatives and other agents as required by the Research Project or to otherwise accomplish the purpose of this Agreement. Such information or data will not be disclosed to non-Government personnel except under a separate non-disclosure agreement and with the written permission of the reporting party. If any party learns of an actual or potential unauthorized use or disclosure of the other party (s) proprietary information, such party will promptly notify the other party and at such party (s)'s request, provide such other party with reasonable assistance to recover the proprietary information and to prevent subsequent unauthorized uses or disclosures of such information.

MEMORANDUM OF UNDERSTANDING BETWEEN THE NATIONAL NAVAL MEDICAL CENTER, BETHESDA, MARYLAND, WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC AND NIGHT VISION ELECTRONIC SENSORS DIRECTORATE, FT. BELVOIR, VIRGINIA

C. Limitation. No party will have any confidentiality obligation with respect to the confidential information belonging to or disclosed by the other parties that:

1. The parties independently knew or developed before receiving the confidential information from the other party.
2. The parties lawfully obtained from another person under no obligation of confidentiality.
3. Is or becomes publicly available other than as a result of an act or omission of such party or any of its employees, agents or representatives.
4. Is related to potential hazards or cautionary warnings associated with the production, handling or use of the subject matter of the Research Plan.

IV. Resources. The parties do not anticipate any transfer of funds associated with this Agreement. Each party will apply its resources in accordance with its established missions and priorities, and provide benefit to the other parties only through collaboration.

V. LIABILITY. Inasmuch as NNMC, WRAMC and NVESD are all instrumentalities of the United States, all claims arising hereunder will be handled in accordance with the Federal Tort Claims Act (FTCA). NNMC, WRAMC and NVESD will cooperate in the investigation of any claims. In the event that a claim or lawsuit is filed, or that an adverse medical outcome requires an investigation, the party with responsibility over the site of where the alleged negligence occurred will be responsible for investigating the allegations and adjudicating the claim or lawsuit, with the other parties agreeing to cooperate in the investigation. This MOU is not intended, and should not be construed, to create any right or benefit, substantive or procedural, enforceable at law or otherwise by any third party against the parties, their parent agencies, the U.S., or the officers, employees, agents or other associated personnel thereof.

VI. PATENTS. All inventions conceived or first actually reduced to practice under this MOU by a government employee shall be reported in accordance with the inventor/employee's standard invention reporting practices and procedures and, for NNMC employees to the Staff Judge Advocate's Office, who will coordinate with the NNMC/Patent Counsel for the Naval Medical Research Center. Upon receipt of a disclosure, counsel shall confer and determine who shall prepare the application and decide, subject to review by higher authority, upon a division of royalties, as appropriate.

VII. PROTECTED HEALTH INFORMATION. All institutions acknowledge that DOD 6025.18-R (Health Information Privacy Regulation) and the Health Insurance Portability and Accountability Act (HIPAA) at 45 CFR Parts 160 and 164 govern the use and disclosure of protected health information and, as appropriate will comply with these requirements, as well as the HIPAA security standards as set forth in DOD 8580.02-R. In accordance with 45 CFR §164.501 "Research" means a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.

MEMORANDUM OF UNDERSTANDING BETWEEN THE NATIONAL NAVAL MEDICAL CENTER, BETHESDA, MARYLAND, WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC AND NIGHT VISION ELECTRONIC SENSORS DIRECTORATE, FT. BELVOIR, VIRGINIA

With respect to such use or disclosure of Protected Health Information ("PHI"), the parties agree as follows:

1. The parties shall use or disclosure PHI for Research purposes in compliance with HIPAA and the Privacy Rule and the federal regulations governing the conduct of human subject research.
2. For any use or disclosure of PHI for Research purposes, the Parties shall cooperate to obtain an appropriate subject authorization to allow such use or disclosure of PHI to the parties to perform the Cooperative Work and to obtain any reviews or approvals by the Parties' respective IRBs. Such authorization shall authorize the NNMCMC and WRAMC to disclose PHI to the following persons or groups of individuals: NVESD personnel (as needed for this study), collaborators, agents, and representatives, the IRB(s) that may review the procedures and protocol for this study, any regulatory agencies with jurisdiction over the Collaborative Work, and other Investigators and personnel, including those at a different facility that are also participating in the Collaborative Work. The collaborator shall not disclose PHI to a third party without appropriate Subject authorization.

VIII. **REVIEWS.** This agreement will be reviewed annually on the anniversary date, at which time it may be modified, cancelled or renegotiated. Additionally, it may be modified, cancelled or renegotiated upon 30 days written notice when deposited in the United States mail and directed to the other party or earlier by mutual consent.

IX. **AMENDMENTS.** It is agreed that the changes to this MOU, except for dates, must be forwarded to all parties: NNMCMC, Responsible Conduct of Research Service, 8901 Wisconsin Avenue, Bethesda, Maryland 20889-5612; Walter Reed Army Medical Center, Washington, DC and Night Vision Electronic Sensors Directorate, Ft. Belvoir, Virginia in the form of an amendment signed by authorized agents of all the organizations.

X. **EFFECTIVE PERIOD.** The effective period of this MOU shall be from the date executed to April 30, 2012.

The parties acknowledge that a number of changes are currently underway that may potentially effect this agreement and may require that it be reauthorized and/or modified. Pursuant to the 2005 Base Realignment and Closure (BRAC) Commission's recommendations, Walter Reed Army Medical Center (WRAMC) will relocate all tertiary (sub-specialty and complex care) medical services to NNMCMC, establishing NNMCMC as the Walter Reed National Military Medical Center (WRNMMMC), Bethesda, Maryland. All BRAC-related construction is mandated to be completed by September 15, 2011. While no specific date has been set at this time for the establishment of WRNMMMC, it is anticipated that this will occur sometime prior to September 15, 2011. Additionally, NNMCMC is part of the Joint Task Force National Capital Region-Medical (JTF CAPMED), which the Deputy Secretary of Defense established in September 2007 to oversee the delivery of integrated healthcare in the National Capitol Area. As part of its work, during the lifetime of this agreement, JTF CAPMED may take on more of a role with respect to research done at NNMCMC. Consequently, NNMCMC's commitment to continued participation is subject to the above caveats.

MEMORANDUM OF UNDERSTANDING BETWEEN THE NATIONAL NAVAL MEDICAL CENTER, BETHESDA, MARYLAND, WALTER REED ARMY MEDICAL CENTER, WASHINGTON, DC AND NIGHT VISION ELECTRONIC SENSORS DIRECTORATE, FT. BELVOIR, VIRGINIA

XI. TERMINATION. This agreement will continue in effect until the expiration of the effective period as indicated in section X or until it is cancelled as described by section VIII.

XII. It is further understood that Chief, Bureau of Medicine and Surgery and Army equivalent will have the right to terminate this agreement immediately upon written notice in the event of war or national emergency. The Commanders at NNMC and WRAMC may also be able to terminate the agreement immediately upon written notice in the event of war or national emergency. NVESD's termination of the agreement is subject to the provisions in its federal grant.

XIII. CONCURRENCE. All parties to this MOU concur with the level of support and resource commitments.

XIV. FUNDING. The parties' participation in the underlying research and in the MOU are subject to the availability of funds to the extent that funds are expended. This MOU is not an obligation or commitment of funds, nor a basis for transfer of funds, but rather is a basic statement of the understanding between the parties hereto of the tasks and methods for performing the tasks described herein. Unless otherwise agreed in writing, each party shall bear its own costs in relation to this MOU. Expenditures by each party will be subject to its budgetary processes and to the availability of funds and resources pursuant to applicable laws, regulations, and policies. The parties expressly acknowledge that the above language in no way implies that Congress will appropriate funds for such expenditures.


XV. POINTS OF CONTACT:

Walter Reed is COL Kraig S. Bower, MC, USA

NNMC is CDR David L. Cute, MC, USN

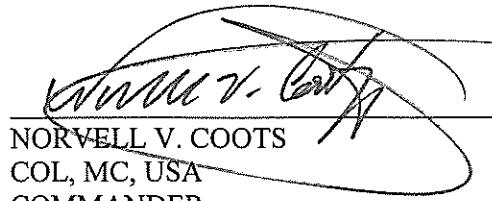
NVESD is Mr. Brian S. Miller

XVI. CONCURRENCE. It is agreed that this written statement embodies the entire agreement of the parties regarding this affiliation, and no other agreements exist between the parties regarding this work except as expressed in this document. All parties to this agreement concur with the level of support and resource commitments that are documented herein.



M. L. NATHAN
Rear Admiral, Medical Corps
United States Navy
COMMANDER
NATIONAL NAVAL MEDICAL CENTER

DATE: 2/8/10



NORVELL V. COOTS
COL, MC, USA
COMMANDER
WALTER REED ARMY MEDICAL CENTER

DATE: 24 Feb 10

WS Fenner

A. FENNER MILTON
DIRECTOR
NIGHT VISION ELECTRONIC SENSORS
DIRECTORATE
FT BELVOIR, VIRGINIA

For

DATE: 12 MARCH 2016

MEMORANDUM FOR CHIEF, RESEARCH REVIEW SERVICE

DEPT OF CLINICAL INVESTIGATION, WRAMC

1. **SUBJECT:** Request for Change in Protocol (Addendum)

- a. IRBNet # 20481
- b. Optical Quality, Threshold Target Identification, and Military Target Task Performance after Advanced Keratorefractive Surgery
- c. Principal Investigator: COL Kraig S. Bower, MC, USA
Service: Ophthalmology
Department: Surgery
Contact: 202-782-0202
Protocol Type: H-GMR

2. **THE PROGRESS IN APPROVED EXPERIMENTS, TO INCLUDE PAST PRODUCTIVITY:**

To date no patients have been enrolled in this study. Due to the protocol approval process at NNMC and HRPO, numerous changes were requested prior to final approval. We are now requesting approval from WRAMC DCI for changes in the protocol recommended by NNMC and HRPO.

3. **EXPLANATION OF THE PLANNED EXPERIMENTS TO BE UNDERTAKEN OR MODIFICATIONS OF THE STUDY:**

There were numerous changes to the protocol and consent form requested by both NNMC and HRPO. Major changes to the protocol and consent form are listed below while a listing of recommended revisions and comments from both NNMC and HRPO are attached.

- 1. **Study Phases:** The study will be conducted in 3 sequential phases based on additional testing required which will allow more timely reporting of results:
PHASE I: Recruitment of 112 patients (28 WFG PRK, 28 WFO PRK/ 28 WFG LASIK, 28 WFO LASIK) who will undergo only psychophysical testing
PHASE II: Recruitment of 56 patients (14 WFG PRK, 14 WFO PRK/ 14 WFG LASIK, 14 WFO LASIK) who will undergo psychophysical testing and testing at the night firing range
PHASE III: Recruitment of 56 patients (14 WFG PRK, 14 WFO PRK/ 14 WFG LASIK, 14 WFO LASIK) who will undergo psychophysical testing and testing at the night vision lab
- 2. **Randomization:** The surgical procedure (PRK & LASIK) will no longer be randomized. The subject will elect to undergo either LASIK or PRK based on a discussion between

themselves and the doctor. Patients will still be randomized to receive either wavefront guided or wavefront optimized ablation. As a result, the Thin Cornea Group (112 subjects) will no longer be needed and the total number of patients in this study will be 224. Statistical power calculations conducted in the initial design of this study did not include the 112 subjects in the thin cornea group and the elimination of this group will not affect our ability to determine if a significant difference exists between procedure and ablation type.

3. **Modified & Clarified the number of Consent Forms:** All four consent forms were merged into one consent form which includes a description of each study phase. Patients will know which phase they will be enrolled in prior to enrollment so they can be directed to additional costs, risks etc specific to them. Risks associated with the procedures themselves are not listed in the consent form for the study as these risks are already listed in a separate refractive surgery consent form detailing surgical risks.
4. **Subject recruitment process:** The subject recruitment process was poorly described in the original protocol. No changes in the recruitment process has occurred; however, the process is described more accurately and we clarified the what determined a subject's eligibility to be a study subject (availability of returning WRAMC for follow-up evaluations and no scheduled PCS moves).
5. **Ombudsman:** The role of the ombudsman was not described in the original protocol. We have included the ombudsman in this version of the protocol.
6. **Subject screening** The order and timing of these activities of the subject screening, clinical evaluation, and the informed consent process is clarified.
7. **Location of WFG surgery:** The Study Design now indicates that surgery for subjects randomized to WFG will be conducted at NNMC as indicated in the consent documents.
4. **COMMENTS ON WHETHER THE MODIFICATIONS WILL INCREASE RISKS TO PARTICIPANTS ENROLLED IN THE STUDY:** None.
5. **SUMMARY OF PAST SPENDING AND JUSTIFICATION FOR ADDITIONAL FUNDING:** No additional funds requested.
6. **NUMBER OF SUBJECTS ENROLLED (OR ANIMALS) TO DATE:**

WRAMC subjects enrolled: 0
NNMC subjects enrolled to date: 0
Study-wide enrolled: 0

7. **JUSTIFICATION FOR ADDITIONAL SUBJECTS (OR ANIMALS) AND METHOD OF RECRUITMENT FOR SUBJECTS:**

N/A

Attachments:

1. For Human Use Study – Include 1) an electronic copy of the proposed consent form (s) and/or HIPAA(s) with all changes highlighted in YELLOW; and 2) a copy of most recent approved consent form(s) and/or HIPAA(s).
2. For Animal Use Study – A copy of the Animal Use and Care Committee's approval for this addendum.

The Principal investigator signature will be provided electronically prior to the submission of the document

"Electronic Signature Notice: In accordance with the "Government Paperwork Elimination Act" (GPEA) (Pub.L. 105-277; codified at 44 USC 3504); Federal and DOD applicable instructions, directives and regulations, documents have been electronically signed and authorized by all who have been required to do so. These signatures have the same effect as their paper-based counterparts. Verification is retained within our protected electronic records and audit trails."

**WALTER REED ARMY MEDICAL CENTER
WASHINGTON, D.C**

This Clinical Trial consent form is valid only if it contains the IRB stamped date.

**Consent for Voluntary Participation in a Clinical Trial (a type of research study) Entitled:
“Optical Quality, Threshold Target Identification, and Military Target Task Performance
After Advanced Keratorefractive Surgery”.**

**Principal Investigator: COL Kraig S. Bower, MC, Ophthalmology Service, Department of
Surgery, phone (202) 782-0202.**

Study Site: ☒ NNMC, ☐ MGMC, ☒ WRAMC, ☐ USUHS

1. INTRODUCTION OF THE STUDY

You are being asked to be in this research study because you are an active duty U.S. Army Soldier, age 21 or older, will be located in the national capital region for at least 1 year, and wear either glasses or contact lenses for either nearsightedness and/or astigmatism (unequal curvature of the eyeball). Your participation is voluntary. Refusal will not result in any penalty or loss of benefits to which you are otherwise entitled, nor will refusal have any affect on your military career status.

2. PURPOSE OF THE STUDY

The purpose of this research project is to evaluate the outcomes of visual performance in nighttime military settings before and after receiving wavefront guided or wavefront optimized laser assisted in situ keratomileusis (LASIK) or photorefractive keratectomy (PRK) surgery. Although daytime vision is often excellent following refractive surgery, there have been reports of night vision changes resulting from PRK and LASIK.

Studies have shown LASIK and PRK to be safe and effective in the treatment of nearsightedness, farsightedness and astigmatism (e.g. corneal or refractive power asymmetry) in civilians and in U.S. Army personnel. In nearsightedness, farsightedness or astigmatism, the clear front surface of your eye, the “cornea”, does not have the proper focusing power. To correct this deficiency you must wear lenses, either glasses or contacts, either in front of the cornea or on the cornea in order to see clearly. Both LASIK and PRK use a machine called an excimer laser to reshape your cornea to try and give it the proper focusing power. In the LASIK procedure a “flap” is made in the cornea using another laser, called a femto-second laser. The flap is lifted and the excimer laser is used to reshape the cornea underneath. The flap is then replaced and allowed to heal. In the PRK procedure no flap is made. Instead, the outer layer of cells on the clear part of your eye, the corneal epithelium, is removed exposing the layer to be treated by the laser. Use of both lasers to make the flap and reshape the cornea is approved by the Food and Drug Administration (FDA) and the procedure is not considered investigational (experimental). These are the exact same procedures that other soldiers are receiving at WRAMC & NNMC and are considered ‘standard of care.’

Both LASIK and PRK surgeries can be either wavefront guided or wavefront optimized. The

WRAMC IRB	ID #	20481-3(add2)	Approved on:	2/12/2010
			Expires on:	8/11/2010

WRAMC IRB ID #	20481-3(add2)	Approved on:	2/12/2010
		Expires on:	8/11/2010

wavefront guided procedure customizes the laser treatments based on the individual characteristics of the eye being corrected. The wavefront optimized procedure uses laser treatment software that has been designed with certain wavefront corrections pre-programmed, and a customized wavefront plan is not employed.

3. PROCEDURES TO BE FOLLOWED

This study will be conducted in three sequential phase. You will only be in a single phase. The phase you are in will depend upon when you agree to be in the study.

Phase I will consist of a preoperative evaluation and testing at WRAMC, the surgery either at WRAMC (wavefront optimized) or NNMC (wavefront guided), and post-operative evaluations at WRAMC. Phase I will consist of a total of 112 subjects.

Phase II will consist of a preoperative evaluation and testing at WRAMC, a pre-operative indoor M16 night fire range at Ft. Belvoir, the surgery either at WRAMC (wavefront optimized) or NNMC (wavefront guided), and post-operative evaluations at WRAMC and post-operative M16 night fire range at 6 wks and 6 mos. Your marksmanship skill will be evaluated with an M16-A2 rifle on a modified range under low light or nighttime conditions. The purposes of these tests are to evaluate the effect of the types of surgeries on night vision in a military environment. You will undergo testing in the night firing range at the Night Vision and Electronic Sensors Directorate at Ft. Belvoir a total of three times (before surgery, 6 weeks and 6 months after surgery). You will need to arrange your own transportation to Ft. Belvoir and this will result in some cost to you if you use a POV. Testing will be during normal business hours in a facility that simulates nighttime conditions. Phase II will consist of a total of 56 subjects.

Phase III will consist of a preoperative evaluation and testing at WRAMC, a pre-operative computer simulation at Ft. Belvoir requiring you to identify images of military vehicles at Ft. Belvoir, the surgery either at WRAMC (wavefront optimized) or NNMC (wavefront guided) post-operative evaluations at WRAMC and post-operative computer simulation requiring you to identify images of military vehicles at Ft. Belvoir. The training and testing you will receive will consist of identifying and recognizing thermal images of military vehicles displayed on a computer monitor. Vehicles will be at various resolutions and in different background environments, simulating real world nighttime conditions. Your responses will be scored and evaluated. The purposes of these tests are to evaluate the effect of the types of surgeries on night vision in a military environment. You will undergo testing in the Human Perception Laboratory at the Night Vision and Electronic Sensors Directorate at Ft. Belvoir a total of three times (before surgery, 6 weeks and 6 months after surgery). You will need to arrange your own transportation to Ft. Belvoir and this will result in some cost to you if you use a POV. You will also be required to pass a pretest each time before you can begin testing. The pretest will ascertain if you know the military vehicles well enough to undergo testing. If you do not pass the pre-test, you will not be allowed to test. Testing will be during normal business hours in a facility that simulates nighttime conditions. Phase III will consist of a total of 56 subjects.

All Phases

If you agree to be in this study you will be randomly assigned (similar to the flip of a coin) to receive either a wavefront optimized ablation pattern or a wavefront guided ablation pattern. You will NOT be randomly assigned either PRK or LASIK and that decision will be up to you and your doctor. Your

WRAMC IRB ID #	20481-3(add2)	Approved on:	2/12/2010
		Expires on:	8/11/2010

chances of being assigned to each group are equal. Depending on your assigned group, you will be treated at either the Walter Reed Army Medical Center Refractive Surgery Clinic or the NNMC at Bethesda. If you are receiving surgery at NNMC, you may drive directly to NNMC on the day of surgery, but depending on where you are traveling from, you may incur additional cost. For your convenience, you may park at WRAMC, take a shuttle bus to NNMC, undergo surgery, and return to WRAMC via the shuttle bus. The shuttle bus leaves every 30" on the hour and 1/2 hour in front of the main lobby on the first floor.

Demographic data, such as age and gender, will be collected during your screening exam in order to provide a correlation with clinical data. You will undergo eye testing before surgery and at 1, 3, 6 and 12 months after the surgical procedure at Walter Reed Army Medical Center as part of the standard of care (SOC). This will involve measuring vision, refraction (the need for glasses), eye pressure, corneal (the clear transparent outer layer of the eye) curvature, corneal clarity, corneal thickness, and contrast sensitivity [the ability to distinguish vertically oriented lines of different sizes and levels of contrast (e.g. black & white v. shades of gray)]. On several examinations, some of these tests will be repeated after your eyes have been dilated with eye drops.

As part of this study, you will be asked to undergo some additional eye testing for research purposes at the eye examination before surgery and at the examinations done 1, 3, 6, and 12 months after surgery. Your vision will be measured using standard visual acuity chart and 2 charts with low contrast letters (e.g. low contrast=faded, light grey letters). You will also be asked to complete a questionnaire before surgery and 1, 3, 6 and 12 months after surgery to determine your satisfaction with your laser eye surgery. It will take you approximately 5 minutes to complete the questionnaire each time it is given. A topographic (surface) map of your eye will be obtained using a Wavefront Analyzer. Contrast sensitivity will be measured using a computer, which displays spatial gratings (e.g. vertical stripes) on a monitor. The computer will vary the size of the vertical stripes and the level of contrast of the stripes (e.g. black & white v. shades of gray). Your task will be to identify which side of the monitor the spatial grating appears. This will take you approximately 20 minutes to complete. Each clinic appointment will last from one to two hours.

If you are a woman capable of having children, you will be asked to have a urine pregnancy test before the surgical procedure. If this test is positive, you will not be able to continue in this study. Additionally, if you plan to become pregnant in the next 12 months you can not be in this study since pregnancy has been shown to cause a change in the spectacle prescription.

4. AMOUNT OF TIME FOR YOU TO COMPLETE THIS STUDY

You will be part of this study for slightly more than 12 months. The amount of time required to complete this study will depend on which phase of the experiment you take part in.

Phase I, Phase II, and Phase III: During phase I, you will be asked to visit the WRAMC clinic up to 10 times. Additionally, if you are randomized to receive WFG surgery, you will have to go to the NNMC to receive surgery. You will be seen at WRAMC the day after surgery, 3 or 4 days after surgery, and one week after surgery. Each visit will last about 15 to 30 minutes. Additional follow-up evaluations will be at 1 month, 3 months, 6 months and 12 months following your surgery. These

WRAMC IRB ID # 20481-3(add2)	Approved on:	2/12/2010
	Expires on:	8/11/2010

visits will last up to 1 to 2 hours each. Over the entire twelve months, this will require as much as 10 hours of examination time after the surgery (postoperatively). The standard amount of time for patients not involved in research is about eight hours. Research candidates can expect an additional two hours of testing.

Phase II: In addition to your follow-ups at WRAMC, you will be asked to fire an M16 at a range at Ft. Belvoir preoperatively, at 6 weeks post-operatively, and at 6 months post-operatively. You will not be asked to qualify at this range, but to shoot at a target located at variable distance from you location. This requirement is expected to take approximately 60 minutes. The standard amount of time for patients not involved in research is about eight hours. Research candidates in phase II can expect an additional 5 hours of testing.

Phase III: In addition to your follow-ups at WRAMC, you will be asked to visit the Night Vision Laboratories a total of 3 times (before surgery and at 6 weeks and 6 months after surgery) to participate in the night vision sensor testing. You will be provided training software to complete on your own. This will take approximately 4 hours. Prior to testing at Ft. Belvoir you will undergo refresher training that may last up to 4 hours, depending on your skill. The testing period will last up to 3 hours. Research subjects in Phase III can expect to expend an extra 21 hours of testing.

5. NUMBER OF PEOPLE THAT WILL TAKE PART IN THIS STUDY

There will a total of 224 people in total taking part in this study. A total of 112 will be enrolled in phase I, 56 patients will be in phase II, and 56 patients will be in phase III.

6. POSSIBLE RISKS OR DISCOMFORTS FROM BEING IN THIS STUDY

There are no significant risks that may develop as a result of participation in this study other than those associated with the surgery itself. Given that the surgery is NOT experimental and would be performed as standard of care outside of this research project, those risks are not addressed in the research consent form. The surgeon will discuss the risks associated with the surgery when you review the surgical consent form. None of the testing procedures pose any risk beyond a normal eye examination, viewing a computer monitor, or military training.

Any additional risks that may develop as a result of your participation in this study, other than those associated with the procedure itself are related to the M16-A3 night firing range. Military personnel trained in the use of night vision devices and small arms range activities will supervise all operations of this part of the study. Strict adherence to all range safety instructions will mitigate any risk of injury. The risks of injury are expected to be similar to those of any military supervised rifle range activity.

None of the contrast sensitivity (the ability to distinguish vertically oriented lines of different sizes and levels of contrast (e.g. black & white v. shades of gray)) testing or the night vision sensor testing has any risks other than those associated with looking at a computer monitor. However, because of the travel required to Ft. Belvoir in addition to the required pre-test training, Phase III has the largest time commitment of the three phases. This will be further discussed on the NVESD Informed consent. Additionally, you may incur additional costs associated with driving to Ft. Belvoir.

WRAMC IRB ID #	20481-3(add2)	Approved on:	2/12/2010
		Expires on:	8/11/2010

While all risks that we know about have been listed above, other risks about which we do not know may occur or be discovered during future studies. If we find that there was a major risk to you that was not known at the time of your participation in the study, and the risk might have some effect on your health, you will be informed.

7. POSSIBLE BENEFITS FROM BEING IN THIS STUDY

The information we gain from you being in will help us gain important knowledge regarding the visual performance of Soldiers who receive the wavefront optimized and wavefront guided surgery. This knowledge will assist us in providing the best possible refractive surgery procedures to future Soldiers.

8. CONFIDENTIALITY/PRIVACY OF YOUR IDENTITY AND YOUR RESEARCH RECORDS

The principal investigator will keep records of your being in this study. These records may be reviewed by individuals from the Walter Reed Department of Clinical Investigation (DCI), the Institutional Review Board and the Responsible Conduct of Research Service at the NNMC, the Walter Reed Human Use Committee (HUC), Human Research Protection Office (HRPO) of the U.S. Army Medical Research & Materiel Command (USAMRMC), the Army Clinical Investigation Regulatory Office (CIRO), and other government agencies as part of their duties. These duties include making sure that research subjects are protected. Collaborators of the study will not have access to your medical records. Confidentiality of your records will be protected to the extent possible under existing regulations and laws. Complete confidentiality cannot be promised, particularly for military personnel, because information bearing on your health may be required to be reported to appropriate medical or command authorities. Your name will not appear in any published paper or presentation related to this study.

When you enter this study you will be given a study ID number which will not contain any part of your social security number. This study ID number, not your name or social security number, will be used to label your data for analysis. However, because you are also a patient we will maintain your name and personal information in your study (paper) chart. This will assist us in prescribing you medication if you might need it. The randomization table linking your study ID number with your personal identifying information will be kept in a locked file in the Walter Reed Center for Refractive Surgery, and access to it will be restricted to the principal investigator and his designee(s). All clinical and research data will be kept for 7 years.

This research study meets the confidentiality requirements of the Health Insurance Portability and Accountability Act (HIPAA). A HIPAA authorization form for this study will be provided to you separately, and you will be asked to sign that form.

9. CONDITIONS UNDER WHICH YOUR PARTICIPATION IN THIS STUDY MAY BE STOPPED WITHOUT YOUR CONSENT

Your taking part in this study may be stopped without your consent if remaining in the study might be dangerous or harmful to you. Your taking part in this study may also be stopped without

WRAMC IRB ID #	20481-3(add2)	2/12/2010	8/11/2010
		Approved on:	Expires on:

your consent if the military mission requires it, or if you become ineligible for medical care at military hospitals. The principal investigator may terminate your participation in this study if you fail to attend the baseline or follow-up examinations or elect not to undergo the laser procedure.

10. ELIGIBILITY AND PAYMENT FOR BEING IN THIS STUDY

You will not be paid for your participation in this research study.

11. COMPENSATION IF INJURED AND LIMITS TO MEDICAL CARE

Should you be injured as a direct result of being in this study, you will be provided medical care for that injury at no cost to you. You will not receive any compensation (payment) for injury. You should also understand that this is not a waiver or release of your legal rights. You should discuss this issue thoroughly with the principal investigator before you enroll in this study.

Medical care is limited to the care normally allowed for Department of Defense health care beneficiaries (patients eligible for care at military hospitals and clinics). Necessary medical care does not include in-home care or nursing home care.

12. COSTS THAT MAY RESULT FROM TAKING PART IN THIS STUDY

There are no additional costs for taking part in this study other than returning to WRAMC for your follow-up appointments, driving to Ft. Belvoir, or lost duty time. Additionally, if your surgery is conducted at NNMC, you can either park at WRAMC on the day of surgery and take a government sponsored shuttle-bus (leaves on the half-hour) or you can drive directly to NNMC.

13. IF YOU DECIDE TO STOP TAKING PART IN THIS STUDY AND INSTRUCTIONS FOR STOPPING EARLY

You have the right to withdraw from this study at any time. If you decide to stop taking part in this study, you should tell the principal investigator as soon as possible. By leaving this study, you do not risk losing your right to medical care. Some testing or period of observation by the investigators may be recommended for you in order for you to safely stop taking part in this study. Any new significant finding during the course of this study that might affect your willingness to continue participation will be communicated to you.

14. STEPS TAKEN BEFORE AND DURING THIS STUDY TO PROTECT YOU

The surgery will be conducted according to manufacturer's guidelines and in the same way as it would be done if you were not taking part in this study. Additionally, we will follow the "standard of care" or "best clinical practices" in all preoperative and postoperative evaluations and you will be carefully monitored for complications of the surgery. Any undesired, clinically significant change in the eye or eyes operated on will be evaluated and treated by investigators.

To monitor for glaucoma, your intraocular pressure (pressure inside the eye) will be measured while you are taking topical steroid drops. We will use a technique called applanation tonometry with either a tonopen or a Goldmann Applanation tonometry. These devices measure the pressure inside your eyes by gently touching the front of your eyes until a predetermined circular area is achieved. Your post-operative medications will be changed when necessary if your eye pressure is significantly

WRAMC IRB ID #	20481-3(add2)	Approved on:	2/12/2010
		Expires on:	8/11/2010

increased.

If you are pregnant or if you plan to become pregnant, you will not be eligible for surgery. Women of childbearing age must take a urine pregnancy test before starting this study. The order for the pregnancy test will be submitted during the preoperative evaluation. The pregnancy test must be completed by an accredited US Army Laboratory. You can either do it at the WRAMC lab which located down the hall from CRS or you can complete the test at the lab located at your home station. If this test is positive, you cannot take part in this study.

15. WHAT ARE THE UNKNOWN RISKS TO YOU OR AN UNBORN CHILD/FETUS

It is not known whether this treatment or the medication associated with the surgery might harm an unborn child. Therefore, you should not be in this study if you are pregnant. Also, you should not be in this study if you are breast-feeding since the medications may be passed from mother to child. A period of six month must elapse from the cessation of breast feeding before a soldier is eligible for refractive surgery. This is a requirement for ALL refractive surgery patients, not just refractive surgery patients. This is to ensure refractive stability has been achieved.

You should avoid becoming pregnant while you are taking part in this study as it has been shown that pregnancy can change a patient's spectacle prescription. If you plan to become pregnant during the study period, you are not eligible for surgery as a study subject. Please inform the research director and you may receive surgery as a regular patient. However, you should avoid becoming pregnant for at least six months after receiving the treatment. The reason for avoiding pregnancy for at least 6 months after the surgery is because of the possibility that re-treatment may be necessary

To avoid becoming pregnant you should either have no sexual relations or use a reliable type of birth control. Except for removal of the uterus (womb) for women and vasectomy (surgical cutting of the tubes that carry sperm) for men, birth control methods are not totally effective in preventing pregnancy. The only ways to completely avoid this risk of the treatment to an unborn baby are (1) avoid pregnancy, or (2) do not take this treatment.

16. OTHER PROCEDURES OR TREATMENTS THAT YOU COULD CHOOSE

You may choose to be treated for your nearsightedness without taking part in this study. Should you decide not to participate in this research study, you have the option of continuing to wear either glasses, contact lenses or have these procedures (or other refractive procedure) completed elsewhere. You may also choose to have PRK or LASIK done outside of this study. PRK and LASIK are done at Walter Reed as a standard of care procedures without participation in any research study. Surgical alternatives to PRK and LASIK include laser subepithelial keratectomy (LASEK) and epithelial LASIK (epi-LASIK), radial keratotomy and lens implants. Your doctor can provide you with more information about your nearsightedness, farsightedness and astigmatism and the benefits and risks of the different treatments available. You are encouraged to discuss this with your doctor.

17. IMPORTANT NEW FINDINGS THAT MAY AFFECT YOUR WILLINGNESS TO STAY IN THE STUDY

If we learn new information during the study that could affect your decision to be in this study, we

WRAMC IRB ID #	2/12/2010
	8/11/2010
20481-3(add2)	Approved on:
	Expires on:

will tell you this information. For example, if we learn about new severe side effects of the treatment, we will tell you about these side effects. The results of the research will be provided to you if you so desire.

18. YOUR RIGHTS IF YOU TAKE PART IN THIS STUDY

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care nor will it affect your military career status.

19. CONTACTS FOR QUESTIONS ABOUT THE STUDY

If you have questions about the study, or if you think you have a study-related injury you should contact the principal investigator at 202-782-0202. For questions about your rights as a research participant, contact the Center Judge Advocate at 202-782-1550, Walter Reed Army Medical Center.

A copy of this consent form will be provided to you.

SIGNATURE OF RESEARCH SUBJECT

I have read the information in this consent form. I have been given a chance to ask questions and all of my questions have been answered to my satisfaction.

BY SIGNING THIS CONSENT FORM, YOU FREELY AGREE TO TAKE PART IN THE RESEARCH IT DESCRIBES.

Subject's Signature

Date

Subject's Printed Name

SIGNATURE OF INVESTIGATOR

I have explained the research to the volunteer, or his/her legal representative, and answered all of his/her questions. I believe that the volunteer/subject understands the information described in this document and freely consents to participate.

Investigator's Signature

Date (must be the same as the participant's)

Investigator's Printed Name



REPLY TO
ATTENTION OF

DEPARTMENT OF THE ARMY
WALTER REED HEALTH CARE SYSTEM
WALTER REED ARMY MEDICAL CENTER
6900 GEORGIA AVENUE, NORTHWEST
WASHINGTON, DC 20307-5001


MCHL-CI

15 April 2009

MEMORANDUM FOR COL Kraig S. Bower MC, Ophthalmology Service, Department of Surgery, WRAMC

SUBJECT: Approval of Addendum (#1) to WU # 08-6967 Optical Quality, Threshold Target Identification, and Military Target Task Performance after Advanced Keratorefractive Surgery

1. Your memorandum for Addendum (# 1) dated 12 March 2009 was received by DCI on 18 March 2009 and was reviewed and approved by the Human Use Committee on 14 April 2009 with no revisions. The protocol was originally approved on 12 August 2008.
2. You may incorporate the changes indicated by this addendum upon receipt of this letter.
Enclosed are the approved revised consent forms that must be duplicated and used for enrolling the subjects.
3. If your study has been approved for acceptance of loaned equipment or the provision of an (IND) drug/Placebo, (IDE) device, supplies and/or gift or money or property, you must coordinate this requirement with Ms. Daisy Word, Research Administration Service, DCI, Building #6, Room 4009 at 202-782-7859. Only Pharmacy Service, not the principal investigator, is authorized to receive and dispense drugs.
4. If you have any questions, please contact Ms. Kristin Beltz at 202-782-7848.


Sarathy Komanduri, Ph.D., DAC
Asst. Chief, Research Review Service
Department of Clinical Investigation

Encl
Copy of addendum
HUC minutes to follow

CC: CIRO

MCHL-MOD

DATE: 12 March 2009

MEMORANDUM FOR CHIEF, RESEARCH REVIEW SERVICE**DEPT OF CLINICAL INVESTIGATION, WRAMC****1. SUBJECT:** Request for Change in Protocol

- a. **Work Unit #** 08-6967 (1)
- b. **Protocol Title:** Optical Quality, Threshold Target Identification, and Military Target Task Performance after Advanced Keratorefractive Surgery
- c. **Principal Investigator:** COL Kraig S. Bower, MD, MC
(Rank, Name, Corp)

Title: Director, Center for Refractive Surgery**Department:** Surgery**Phone Number:** (202)782-0202**Service:** Ophthalmology**Fax Number:** (202)782-4653**2. THE PROGRESS IN APPROVED EXPERIMENTS, TO INCLUDE PAST PRODUCTIVITY:**

This protocol was selected to be funded by a CDMRP grant. Due to the administrative requirements of this grant, subject recruitment has not started.

3. EXPLANATION OF THE PLANNED EXPERIMENTS TO BE UNDERTAKEN OR MODIFICATIONS OF THE STUDY:

There are no changes in the planned experiments or in data analysis. We request addition of the Refractive Surgery Center at the NNMC-Bethesda as a collaborating site. NNMC-Bethesda has access to the VISX S-4 IR excimer laser system that we will use for the wavefront-guided (WFG) treatments, and all patients randomized to WFG surgery will have their procedures done at NNMC-Bethesda. This is reflected in the revised CF.

Additionally, because this protocol is now federally funded, we request to recruit subjects in sequential phases. These phases will allow us to report to MRMC intermediate results of this protocol for specific sub-tasks as outlined in the statement of work for the grant.

Patients will be randomized to treatment according to the PLAN in the initial protocol, but the method of testing (e.g. night vision, visual performance at NVESD) will be sequential and not randomized. This change in the design has been reviewed and approved by Robin Howard, DCI Biostatistician.

The 3 phases are:

- 1. 112 Soldiers w/ testing at WRAMC but no additional testing at NVESD. (Phase 1 – no additional testing)
- 2. 56 Soldiers w/follow-up testing at NVESD Night Firing Range (Phase 2 - night firing range)
- 3. 56 Soldiers w/follow-up testing at NVESD Human Perception Laboratory (Phase 3 - visual performance testing)

2

As previously planned, a concurrent sub-protocol will enroll 112 patients with thin corneas who are not eligible for LASIK and will be randomized to either WFG PRK or WFO PRK. This sub-protocol cohort will undergo testing at WRAMC but no additional testing at NVESD. (Sub-protocol – no additional testing)

The consent forms have been modified and there is now a CF for the sub-protocol and one for each randomization block that accurately reflects the study involvement/additional testing for each phase. Those revised CF are attached.

4. COMMENTS ON WHETHER THE MODIFICATIONS WILL INCREASE RISKS TO PARTICIPANTS ENROLLED IN THE STUDY:

There are no additional risks that a subject would incur by this modification.

5. SUMMARY OF PAST SPENDING AND JUSTIFICATION FOR ADDITIONAL FUNDING:

N/A

6. NUMBER OF SUBJECTS (OR ANIMALS) ENROLLED TO DATE:

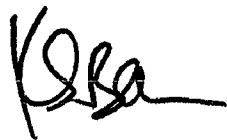
N/A (none so far)

7. JUSTIFICATION FOR ADDITIONAL SUBJECTS (OR ANIMALS) AND METHOD OF RECRUITMENT FOR SUBJECTS:

N/A

Encl. (*As Appropriate*)

1. Overview of study design/block randomization plan modified for the changes requested in this addendum.
2. A copy of most recent approved consent forms (1 for main study and 1 for PRK-only sub-protocol).
3. An electronic copy of the proposed consent form with all changes highlighted.
 - 3a. Phase 1 (No additional testing)
 - 3b. Phase 2 (Night Firing Range)
 - 3c. Phase 3 (Human Perception Lab)
 - 3d. Sub-protocol (PRK only)

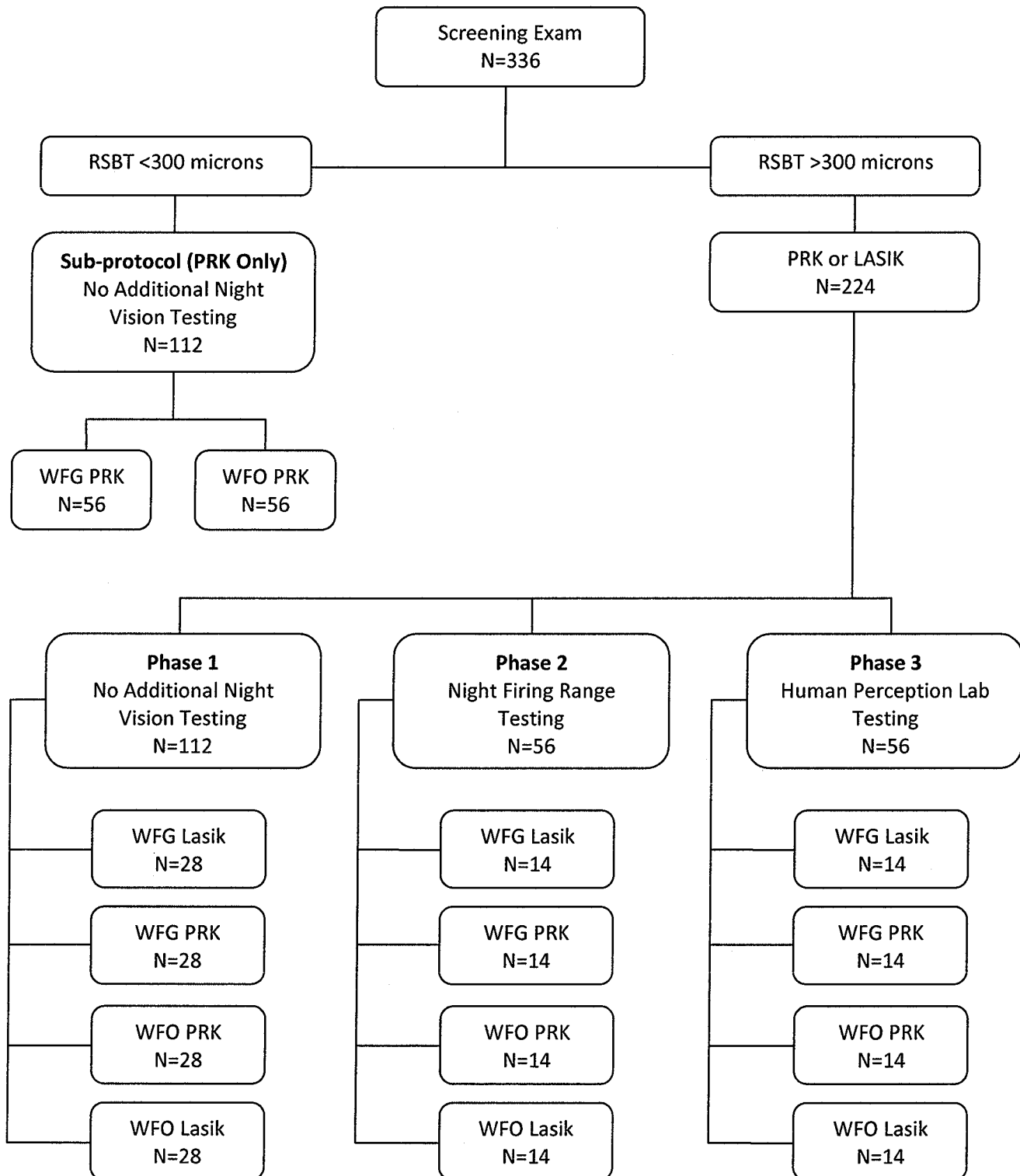


(Signature, Principal Investigator)

Kraig S. Bower, MD, FACS
COL USA MC
Director, Center for Refractive Surgery
Walter Reed Army Medical Center

3

Modified Study Design for WU #08-6967 (Bower) *Optical Quality, Threshold Target Identification, and Military Target Task Performance after Advanced Keratorefractive Surgery*



gave to
Dan 4/15/09 ✓
kl

MCHL- MOD

10 March 2009

MEMORANDUM FOR CHIEF, DEPARTMENT OF CLINICAL INVESTIGATION,
WALTER REED ARMY MEDICAL CENTER

SUBJECT: Request for addition of Associate Investigator

WORK UNIT#: 08-6967

TITLE OF PROTOCOL: Optical Quality, Threshold Target Identification, and Military Target Task Performance after Advanced Keratorefractive Surgery

NEW ASSOCIATE INVESTIGATOR:

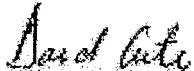
CDR David Cate, DO, USA, MC

Ophthalmology Service, Department of Surgery

Phone: 301-295-1339 Fax: 301-295-1481

Pager: PIN#1702100

E-mail: david.cate@med.navy.mil



Associate Investigator Signature

COL Craig S. Bower, USA MC

Director, Center for Refractive Surgery

Ophthalmology Service, Department of Surgery

Phone: 202-782-0202 Fax: 202-782-4653

Pager: PIN #1653149

E-mail: craig.bower@amedd.army.mil

Current Duty Station: WRAMC

 3/11/2009

Principal Investigator Signature

Reviewed & Approved

(For DCI use after submission)

Attachments:

CV - Cate
CITI Course - Cate



DEPARTMENT OF THE ARMY
WALTER REED ARMY MEDICAL CENTER
WALTER REED HEALTH CARE SYSTEM
WASHINGTON, DC 20307-5001

MCHL-CI

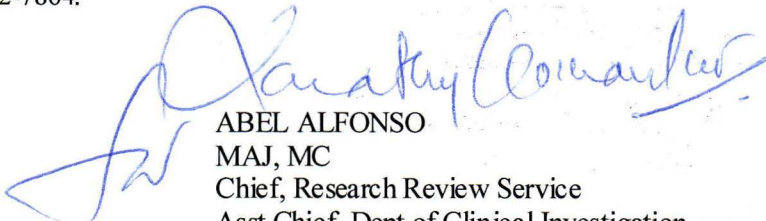
07 November 2008

MEMORANDUM FOR Dr. COL Kraig S. Bower, MC, Ophthalmology Service, Department of Surgery, Walter Reed Army Medical Center, Washington, DC 20307-5001

SUBJECT: Approval of Protocol **Work Unit #08-6967**: Optical Quality, Threshold Target Identification, and Military Target Task Performance after Advanced Keratorefractive Surgery

1. Congratulations! Your protocol was approved with revisions by the Clinical Investigation Committee on 15 July 2008 and by the Human Use Committee (HUC) on 12 August 2008 as a "greater than minimal risk" human use protocol. The last required revisions were received by 6 November 2008. Please use the assigned seven (7) digit **Work Unit #08-6967** for all correspondence with the Department of Clinical Investigation (DCI) regarding this study as noted on item 5 below.
2. The Army Clinical Investigation Regulatory Office (CIRO) approval dated 7 November 2008 was received 7 November 2008. A copy of the minutes from the applicable committee(s) and a final copy of the approved research protocol are attached for your administrative files. **Also, enclosed is the stamped approved consent forms that must be duplicated and used for enrolling subjects and the "STEP-BY-STEP GUIDE..." to be used when consenting subjects.** Your research protocol was approved for a total of 336 subjects who will be enrolled at WRAMC. You may begin work on the project upon receipt of this letter. This approval is only for **one year**. As part of your continuing review and re-approval and in order to keep your research ongoing, you are required to submit an annual progress report (APR) in the first week of July each year.
3. This approval, does not include the Cooperative Research Development Agreement (CRADA) being developed with the Henry M. Jackson Foundation (HMJF) to support this research, therefore, no movement of any CRADA-related resources associated with this study can occur. Only the Pharmacy Service, not the principal investigator, is authorized to receive and dispense drugs.
4. Significant or unexpected side effects must be reported to the Medical Monitor of this study, COL Andrew Eiseman, MC, Asst Chief, Ophthalmology Service, Department of Surgery.
5. As the principal investigator (PI), you are required by Federal, DoD, and WRAMC regulations to submit the following in a timely fashion to the Department of Clinical Investigation if applicable: (a) addenda delineating any changes in the protocol, (b) PI change, (c) notification of serious or unexpected adverse effects within 24 hours, and (d) publication clearance, travel orders and funding requests.
6. Enclosed is a copy of the **NARMC DoD Multiple Project Assurance (MPA) and the WRAMC Federal Wide Assurance that all investigators agree to adhere to in conducting research**, as attested to by your submission of a signed Principal Investigator Responsibilities Statement. If you have any questions, the POC is Ms. Marty Green at (202) 782-7864.

4 Encls
as


ABEL ALFONSO
MAJ, MC
Chief, Research Review Service
Asst Chief, Dept of Clinical Investigation
Co-Chairperson, Human Use Committee



DEPARTMENT OF THE ARMY
U.S. ARMY MEDICAL RESEARCH AND MATERIEL COMMAND
CLINICAL INVESTIGATION REGULATORY OFFICE (CIRO)
ATTN: MCMR-RPC, 1608 STANLEY ROAD
FORT SAM HOUSTON, TEXAS 78234-5055

MCMR-RPC

7 Nov 08

MEMORANDUM FOR Department of Clinical Investigation, Walter Reed
Army Medical Center, ATTN: MCHL-CI (Ms Marty
Green), 6900 Georgia Avenue, NW
Washington, DC 20307-5001

SUBJECT: Protocol Titled, "Optical Quality, Threshold Target
Identification, and Military Target Task Performance after
Advanced Keratorefractive Surgery," by COL Kraig S. Bower, MC
(WU# 08-6967; CIRO# 2009049)

1. Reference:

a. Memorandum, WRAMC, MCHL-CI, 3 Oct 08, Subject:
Forwarding of Research Protocol.

b. Minutes, Human Use Committee, 12 Aug 08.

c. Minutes, Clinical Investigation Committee, 15 Jul 08.

2. The review has been completed of the above referenced
greater than minimal risk study and supporting documents
received 24 Oct 08. The requested revisions to the consent
documents were received on 7 Nov 08 and deemed acceptable. The
study meets regulatory requirements for the protection of human
subjects in research and may commence at Walter Reed AMC.

3. We note that the Principal Investigator has applied for a
Department of Defense Congressionally Directed Medical Research
Program grant through the Peer Reviewed Medical Research
Program.

4. Our point of contact is Ms. Janet LeSage, DSN 471-9325 or
commercial (210) 221-9325.

HAROLD S. SANO

LTC, MS

Deputy Director, Clinical
Investigation Regulatory Office



TABLE OF CONTENTS

Optical Quality, Threshold Target Identification, and Military Target Task Performance after Advanced Keratorefractive Surgery

1.	Protocol Title and Personnel	3
2.	Abstract	5
3.	Objective and Specific Aims	5
4.	Medical Application/ Military Relevance	6
5.	Background and Significance	7
6.	Plan	18
7.	References	32
8.	Facilities/ Organization to be Used	34
9.	Role and Responsibilities of Each Investigator and Collaborator	34
10.	Time Required to Complete the Research	35
11.	Budget	35
12.	Environmental Impact Statement	36
13.	Investigator Compliance Statement	36
14.	Responsibilities of the Principal/ Associate Investigators in Human Subjects Research	37
15.	Medical Monitor Responsibilities	38
16-19.	Signatures	39
20.	Appendices	42

**MEMORANDUM FOR CHIEF, DEPARTMENT OF CLINICAL INVESTIGATION,
WALTER REED ARMY MEDICAL CENTER**

SUBJECT: Application and Request for Approval of Clinical Investigation Study Proposal

1. PROTOCOL TITLE AND PERSONNEL

1.1 Protocol Title:

Optical Quality, Threshold Target Identification, and Military Target Task Performance after Advanced Keratorefractive Surgery

1.2 Principal Investigator

COL Kraig S. Bower, USA MC
Director, Center for Refractive Surgery
Ophthalmology Service, Department of Surgery
Phone: 202-782-0202 Fax: 202-782-4653
Pager: PIN #1653149
E-mail: kraig.bower@amedd.army.mil
Current Duty Station: WRAMC
CITI course date: 18 Jan 2006

1.3 Associate Investigators

LTC Charles D. Coe, USA MSC
Director, Refractive Research
Center for Refractive Surgery
Phone: 202-782-0202 Fax: 202-782-4653
E-mail: charles.coe@amedd.army.mil
Current Duty Station: WRAIR
CITI course date: 7 Feb 2006

LTC Richard D. Stutzman, USA MC
Associate Program Director
Ophthalmology Service, Department of Surgery
Phone: 202-782-8600 Fax: 202-782-6156
E-mail: Richard.stutzman@amedd.army.mil
Current Duty Station: WRAMC
CITI course date: 24 June 2008

Jayson D. Edwards, MD
Research Associate (Contract), Center for Refractive Surgery
Phone: 202-782-3249 Fax: 202-782-4653
E-mail: jayson.edwards@amedd.army.mil
Current Duty Station: WRAMC
CITI course date: 2 Aug 2007

Denise A. Sediq, MS

Research Associate (Contract), Center for Refractive Surgery

Phone: 202-782-0982 Fax: 202-782-4653

E-mail: denise.sediq@amedd.army.mil

Current Duty Station: WRAMC

CITI course date: 7 Nov 2006

Jennifer Eaddy, OD

Staff Optometrist, Center for Refractive Surgery

202-782-0956 phone 202-782-4653 fax

jennifer.eaddy@amedd.army.mil

Current Duty Station: WRAMC

Research Course Training Date: 24 Jan 2006

Chrystyna Kuzmowych, OD

Staff Optometrist, Center for Refractive Surgery

202-782-0981 phone 202-782-4653 fax

chrystyna.kuzmowych@amedd.army.mil

Current Duty Station: WRAMC

Research Course Training Date: 5/11/2006

1.4 Collaborating Personnel**Barbara L. O’Kane, Ph.D.**

US Army RDECOM NVESD

10221 Burbeck. Rd

Fort Belvoir, VA 22060

Phone: (703) 704-3189 DSN 654-3189

Email: Barbara.Okane@nvl.army.mil

Brian Miller, MSME

Chief, Field Performance Branch

Modeling and Simulation Division, NVESD

10221 Burbeck Rd

Fort Belvoir, VA 22060

Phone: (703) 704-2569

Email: brian.miller1@us.army.mil

1.5 Medical Monitor**COL Andrew S. Eiseman, USA MC**

Assistant Chief, Ophthalmology Clinic

Program Director

Ophthalmology Service, Department of Surgery

Phone: 202-782-8087 Fax: 202-782-6256

E-mail: Andrew.eiseman@amedd.army.mil

Current Duty Station: WRAMC

CITI course date: 11 May 2006

2. ABSTRACT

2.1. Purpose: To compare wavefront guided to wavefront optimized laser refractive surgery in terms of visual function, with particular attention to military task performance in patients that receive photorefractive keratectomy (PRK) or Intralase laser assisted in situ keratomileusis (LASIK).

2.2. Research Design: Single-center randomized prospective study done at the Walter Reed Army Medical Center, Center for Refractive Surgery. Collaborative testing for patients enrolled at WRAMC will be done at the Night Vision and Electronic Sensors Directorate at Ft. Belvoir.

2.3. Methodology: A total of 336 subjects will be recruited for this study. 224 nearsighted soldiers will be randomized into one of four treatment groups (56 soldiers per group): Group 1: wavefront optimized photorefractive keratectomy (WFO PRK); Group 2: wavefront optimized laser assisted in situ keratomileusis (WFO LASIK); Group 3: wavefront guided PRK (WFG PRK); and Group 4: wavefront guided LASIK (WFG LASIK). In addition, 112 subjects with thin corneas will be enrolled in a subgroup and randomized to receive WFG PRK or WFO PRK (56 in each group). Subjects will undergo extensive clinical and military visual performance measures both before and after surgery. Outcome measures will include subjective visual performance, objective optical quality, performance predication modeling, and military task performance. Study design will enable comparison of postoperative to preoperative performance as well as comparisons between treatment groups.

Subjective quality of vision will be characterized by standard refractive surgery safety and efficacy outcome measures, including postoperative uncorrected visual acuity, refraction, low contrast visual acuity, and best corrected visual acuity. In addition, the contrast sensitivity function (CSF) will be determined psychophysically using a commercial workstation & software. Analysis will determine the effect on visual performance of the different treatments (WFO PRK vs. WFO LASIK vs. WFG PRK vs. WFG LASIK).

Objective optical quality will be derived from the wavefront aberration map. A Zernike polynomial series will be fit to the wavefront map. Using Fourier optics, a 2-D Modulation Transfer Function (MTF) will be calculated from the wavefront map. Analysis will determine if the objective optical quality of the human eye is affected by different refractive surgery modalities.

Military task performance will be assessed via collaboration with the US Army Night Vision and Electronic Sensors Directorate (NVESD) at Ft. Belvoir. We will use NVESD performance prediction models (the Target Task Performance [TTP] metric) to analyze data derived from the CSF and predict whether there is a significant difference in either the range at which a threshold target identification task can be made or the time a target can be detected. Military task performance will be further evaluated by the NVESD program (threshold target identification) in which tracked vehicle targets will be presented to observers at a sufficient distance to stress the eye response. The percentage of correctly identified stimuli will be plotted as a function of range to produce a psychometric function. Finally, night firing performance will be measured in the night firing tunnel at Ft. Belvoir.

3. OBJECTIVES AND SPECIFIC AIMS

3.1 Overall objective. To determine the effect of two types of wavefront modalities (WFG vs. WFO) and two types of refractive surgery (PRK vs. LASIK) on visual and military task performance after laser refractive surgery.

3.3 Specific objectives:

1. Compare the safety and efficacy of WFG PRK vs. WFG LASIK vs. WFO PRK vs. WFO LASIK in term of standard refractive surgery outcome measures.
2. Compare the four treatment modalities in terms of objective image quality as measured by wavefront aberrometry.
3. Use NVESD performance modeling to predict whether there is a significant difference between treatment modalities in either the range at which target identification task can be made or the time a target can be detected.
4. Compare military task performance after the four treatment modalities in terms of threshold target identification.
5. Compare military task performance after the four treatment modalities in terms of night firing range scores.
6. Compare visual recovery between PRK and LASIK.

3.2 Hypothesis. Previous studies have demonstrated fewer higher order aberrations (HOA) following WFG and WFO treatments when compared to conventional treatments [1-3], after PRK vs. LASIK [4], and Intralase vs. microkeratome LASIK [5-6]. More recent studies have compared HOA and visual outcomes in WVG vs. WFO surgery [7-8]. We hypothesize that WFG surgery will minimize optical aberrations induced by refractive surgery when compared to WFO treatments, thereby minimizing any degradation of objective optical quality following both PRK and LASIK. It is unknown whether such differences will have a meaningful impact on military relevant tasks, however, and thus the importance of this study.

4. MEDICAL APPLICATION/ MILITARY RELEVANCE

Instantaneous life and death decisions are routinely made on the modern battlefield. In this environment, the visual function of the individual soldier will have a critical and direct impact on this decision making process. Glasses in the combat environment have considerable disadvantages: degradation of short term visual performance will occur as dust, sweat, and other substances accumulate on lenses during a mission or patrol; long term visual performance will also diminish as lenses become increasingly scratched and pitted; during periods of intense physical trauma, spectacles can be dislodged from the soldiers face or lost; and, broken spectacles will require replacement which depending on the tactical situation might not be possible. For this reason the Army instituted the Warfighter Refractive Eye Surgery Program (WRESP) in 2000 as a mission readiness asset to units and soldiers, with the Army Medical Command providing approximately 10,000 soldiers a year with free refractive surgery.

Although refractive surgery offers certain benefits on the battlefield when compared to a spectacle correction, it is not without potential disadvantages. As a byproduct of refractive surgery, large amounts of optical aberrations are induced thereby degrading the overall optical quality of the human eye. It is well known that while refractive surgery decreases 2nd order aberrations, it increases the magnitude of higher order aberrations. [9-14] Elevated higher order aberrations have been positively correlated with the decrease in contrast sensitivity and the increase in the symptoms of glare, halos, starbursts, and monocular diplopia. [15-17] However, the relationship between optical quality, characterized by monochromatic aberrations, and visual performance is complex and not perfectly understood. [18-20] Typically, impaired visual function secondary to refractive surgery is only appreciated under mesopic (intermediate lighting - luminance level 10^{-2} to 1 cd/m^2) or scotopic (low lighting - luminance level 10^{-2} to 10^{-6} cd/m^2) conditions where pupil diameter is greatest. It is also in these same conditions (mesopic and scotopic) that most military operations are initiated. In these less than optimal conditions (e.g. night, fog, or dusk) or with degraded vision (e.g. night vision goggles (NVG's), scratched & dirty eye protection) contrast sensitivity can be more important than visual acuity when performing military related tasks such as scanning objects

of different sizes and shapes. [21] To quickly assess and correctly perceive visual tasks such as “Is that shadow on that man’s jacket consistent with a bomb belt? An AK-47? Or perhaps, a loaf of bread?” requires more than just visual acuity.

Recent technology advances have reduced the amount of optical aberrations induced by refractive surgery and resulted in improvements in postoperative quality of vision. The two most prominent advances in this regard are the use of customized wavefront guided (WFG) ablations and the use of a femtosecond laser to create the corneal flap in laser assisted in situ keratomileusis (LASIK). The latter offers better predictability and precision in generating the thin corneal flap, which in turn translates to greater safety and efficacy. However, it is unclear whether these advances offer significant advantages in the military operational environment. While we expect that the improved quality of vision seen in the doctor’s office and clinical trials will result in superior performance in military operational tasks, this hypothesis remains to be tested. The purpose of the present study is to evaluate the outcomes of these state of the art refractive surgery technologies in terms of task performance in a military operational setting.

Another important reason for this study is economic. The money devoted to refractive surgery is fixed. Wavefront guided treatments cost the AMEDD 1.5X more per procedure. Adding in the costs of the IntraLase femtosecond laser increases the costs even more. Therefore an important question to have answered is: Is a soldier’s visual function improved so significantly with wavefront guided ablations and the IntraLase femtosecond laser that it might warrant a decrease in the total number of treatments so that the total cost of refractive surgery to the US Army Medical Command remains constant?

5. BACKGROUND AND SIGNIFICANCE

5.1 Introduction.

Refractive surgery has a proven track record of providing an alternative to spectacle lenses. Since its arrival 15 years ago, the refractive surgery industry has continued to improve its outcomes. Most refractive surgery centers have a success rate of greater than 90% for an eye to achieve 20/20. However, as a byproduct of refractive surgery large amounts of optical aberrations are induced thereby degrading the overall optical quality of the human eye. It is well known that while refractive surgery decreases 2nd order aberrations, it increases the magnitude of higher order aberrations. Elevated higher order aberrations have been positively correlated with the decrease in contrast sensitivity, with objective analysis of the eye’s optical quality revealing up to a two-fold increase in the magnitude of monochromatic aberrations. In addition, patients suffer from an increase in glare, halos, starbursts, and monocular diplopia. However, the relationship between optical quality, characterized by monochromatic aberrations, and visual performance is complex and not perfectly understood.

Several important advances have reduced the amount of higher order aberrations induced by refractive surgery. [22] With the advent of wavefront aberrometry, [23] the potential promise of correcting not only myopia and astigmatism but other, smaller optical aberrations has produced an explosion of research. Wavefront aberrometers are now coupled with computer controlled, flying spot excimer lasers resulting in wavefront guided laser ablations customized to each individual’s eye. Wavefront optimized (WFO) ablations add peripheral treatment to minimize spherical aberration, the principal high order aberration generated by the surgery. Wavefront guided (WFG) surgery measures and treats not only lower order aberrations, such as sphere and cylinder, but also higher order aberrations. Wavefront guided ablations have been shown to reduce the amount of higher order aberrations induced during refractive surgery. [22] Patients treated with wavefront guided laser ablations perform better on contrast sensitivity testing than patients treated with conventional laser treatments. [24]

Another advance in refractive surgery has been the development of a laser to generate the corneal flap needed for LASIK surgery. Traditionally, the corneal flap has been generated by a sharp blade called a microkeratome. Although reliable, most complications associated with the LASIK procedure such as de-centered flaps and incomplete flaps involve the microkeratome. Simply put, the femtosecond laser when compared to a microkeratome not only offers greater safety and efficacy but also better predictability and precision in generating a thin corneal flap of known thickness. [25] This offers two advantages. First, it has been shown that post-operatively, residual astigmatism and visual acuity is significantly better in patients who have had the LASIK procedure with a flap generated by a femtosecond laser. [26] And secondly, the greater precision and predictability of the corneal flap may enhance the effect of a customized wavefront ablation.

Although there are more than 400 reports in the literature investigating various aspects of WFG ablations, [27] no studies exist that either examine the effect of Intralase generated corneal flaps and WFG ablations on visual function and on the performance of vision-dependent military relevant tasks. Because of the extreme and demanding (visual) environment soldiers operate in, WFG ablations and Intralase LASIK might confer advantages that are not evident when analysis is conducted in typical civilian, scientific settings.

The measurement of visual performance in the presence of optical aberrations has a long history in both the civilian and military sectors. [28-33] Typically, these studies investigate the subjective impact of various amounts of optical aberrations on vision with the goal of developing image quality metrics. Conceptually, image quality metrics are simply calculations that predict when an object will appear blurred or clear. Given the inherent costs in designing battlefield imaging systems the U.S. Army Communications and Electronics Command Night Vision and Electronic Sensors Directorate (NVESD) requires robust performance metrics. These performance metrics predict the battlefield performance of (potentially very expensive) imaging systems for various shape and size blurs, good and poor intrinsic target contrast, with various levels and types of noise. The NVESD has a validated a number of robust target acquisition metrics. The Targeting Task Performance Metric (TTP) is one of these metrics. The TTP metric has recently proven to accurately predict the ability of soldiers to identify targets with various types and levels of blur, noise, and contrast degrading the image. [34] As the human eye can be thought of as an imaging system, the same optical aberrations that can adversely affect a thermal imager can also affect a post refractive surgery eye.

In the proposed study a collaborative effort between the Center for Refractive Surgery at Walter Reed Army Medical Center (WRAMC) and the NVESD will explore the relationship between refractive surgery, optical quality, visual performance, and military task performance. The WRAMC Center for Refractive Surgery and NVESD collaboration is uniquely qualified to study this important scientific question. At WRAMC we annually perform over 1,200 refractive surgery treatments on active duty soldiers, many who are enrolled in study protocols. Furthermore, we have sufficient clinical, academic, and military resources within the national capitol area to conduct cutting edge, military relevant research. The NVESD is the leading military research & development center for pilotage and target acquisition systems and has unique expertise and facilities to perform this research. By comparing the most advanced refractive surgery techniques available today on a cohort of soldiers, calculating objective optical quality using NVESD performance metrics, and measuring visual performance with battlefield simulations and weapons ranges, the WRAMC-NVESD collaboration will make not only a very important contribution to the operational readiness of all US Army combat units, but also to the scientific community in their attempt to understand visual performance.

5.2. Technical Background

5.2.1. Subjective Best Focus: The supposed benefit of wavefront guided refractive surgery treatments is a customized ablation pattern that corrects for all the eye's monochromatic aberrations. However, the definition of objective optimal focus is elusive. Are aberrations minimized with a root mean square (RMS) definition of optimal focus? Perhaps optimal focus may be defined by the area maximized under a 2-dimensional MTF or the intensity of the point spread function?

Despite efforts by some of the brightest minds in the vision science community to objectively characterize optimum focus, in the end, the gold standard remains the subjective refraction.

To this end, is subjective best focus more accurately and precisely achieved with either a WFO ablation or a WFG ablation? With LASIK, how important is ablation type (WFO LASIK v. WFG LASIK). Is there any interaction between these variables that might cause a better or worse outcome? Is subjective best focus more reliably achieved with PRK or LASIK?

Refractive surgery outcomes will be defined by the cycloplegic refractions at the 6month post-op. Emmetropia will be the goal in all cases. Outcome measures will be:

1. Accuracy of the Mean Sphere Equivalent (mean error)
2. Precision of the Mean Sphere Equivalent (standard deviation)
3. Accuracy of the Astigmatic correction by the power vectors J0 and J45 [35]
4. Precision of the Astigmatic correction by the power vectors J0 and J45 [35]

5.2.2. Objective Analysis of Optical Quality: A major emphasis of this research is to determine the objective optical quality of the various modes of refractive surgery common today in both civilian and military sectors. Objective analysis of optical quality will be accomplished using a Hartmann-Shack wavefront aberrometer. A wavefront aberrometer can measure the direction of light leaving the eye in 0.2mm increments. From this, the slope of the rays of light leaving the eye can be calculated. A mathematical integration on this slope data will result in the wavefront.

In an eye free of optical aberrations, the wavefront is represented by either a plane or a sphere, depending where along the optical path the wavefront is characterized. In an aberrated eye, however, optical aberrations cause the wavefront to deviate from the planar or spherical wavefront. The difference between the spherical wavefront and an aberrated wavefront is called the wavefront error (**Figure 1**). The wavefront error consists of potentially an infinitely number of points in 3-dimensional space and the Zernike polynomial series is an attempt to organize, quantify, and simplify this massive amount of data.

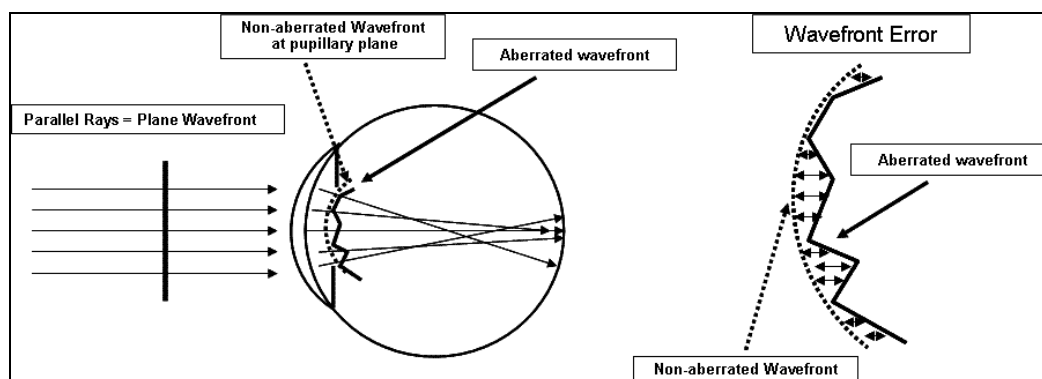


Figure 1. Wavefront error is the difference between a non-aberrated (e.g. perfect) wavefront and an aberrated wavefront. This can be seen on the right side of this figure.

The Zernike polynomial series are a set of basis functions that are orthogonal (e.g. independent) over a unit circle. This attribute is important since any pupil diameter may be normalized and be represented by the unit circle. In addition to being orthogonal, the Zernike coefficients are normalized so that the coefficient of a particular term or mode is the relative RMS contribution to the wavefront error.

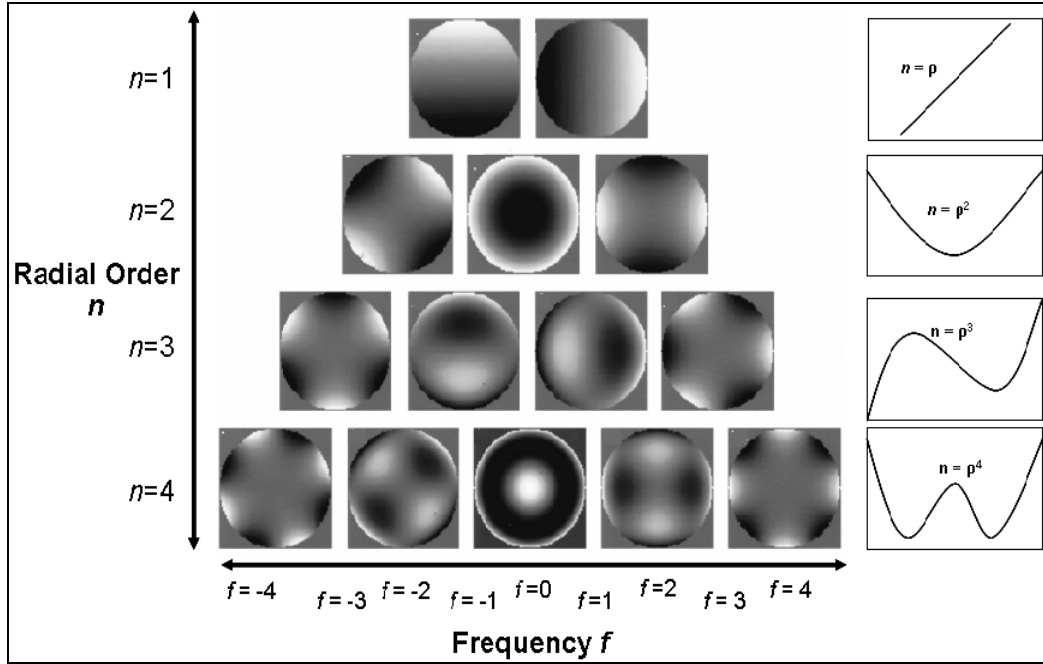


Figure 2. The Zernike Pyramid. The organization and structure of double index notation lends itself to viewing the Zernike polynomial series as a periodic table. Each row equates to radial order and each column represents meridional frequency. The wavefront error is characterized as a function of grey scale. Dark areas denote phase lag, and light areas denote phase advancement (redrawn from Thibos et al [36])

The shape of the wavefront map can be thought of as a sum of these weighted Zernike polynomial terms.

Objective optical quality will be defined by the following parameters:

1. Contrast Sensitivity Function
2. Modulation transfer function
3. Optical transfer function
4. Magnitude of higher order optical aberrations – Total RMS
5. Magnitude of Spherical Aberration
6. Magnitude of Coma

5.2.3. Objective Performance Predictions

A. Introduction: The contrast threshold function (CTF), simply the inverse of the contrast sensitivity function (CSF), is used to evaluate the performance of both a military imaging system and the human visual system. Evaluating the CTF_{sys} in a military imaging system utilizes the CTF_{eye} of an average human eye looking through the imager. The CTF is the visual threshold contrast of sinusoidal patterns when

plotted as a function of spatial frequency and can be related to the Minimum Resolvable Temperature (MRT) measurement. The five imager models provided to the military by the U.S. Army Night Vision and Electronic Sensors Directorate (NVESD) are all based on the CTF, where the radiometry is adjusted for the particular sensor type. The system CTF, for a thermal imager, can be described by:

$$CTF_{sys} = \frac{CTF_{eye}(\xi)}{MTF(\xi)} \left(1 + \frac{\alpha^2 \sigma^2(\xi)}{S_{imp}^2}\right)^{1/2} \quad [\text{unitless}] \quad (1)$$

MTF (ξ) – system modulation transfer function

σ (ξ) – noise filtered in Kelvin by the display and visual system in Kelvin-root seconds

S_{imp} – scene temperature difference that corresponds to half the display brightness (from zero brightness)

α – a calibration factor with units of root hertz

In the NVESD imager models, all systems are considered to be separable in the horizontal and vertical directions. The general CTF calculation provided in equation 1 is in its basic form and includes optical, detector, electronic, and display characteristics.

Two conditions must be considered when evaluating the system performance by the CTF. Sensors operate in conditions in which both noise is visible to the observer, and when it is not. In a noise-limited realm, where $\alpha^2 \sigma^2(\xi) / S_{imp}^2$ is larger than 1, the observer can see noise in the imager, as seen in uncooled

microbolometers, first generation forward looking infrared (FLIR) and second generation FLIR imagers. However, noise is not visible to the observer when $\alpha^2 \sigma^2(\xi) / S_{imp}^2$ is less than 1. The information in the image

is only limited by the CTF_{eye} and image blur, which become the only important components of **Equation 1**. Systems where noise is not a factor include staring InSb sensors, MCT staring sensors and other photon detector systems that have medium to low f-numbers with an associated medium to wide field-of-view (FOV). A requirement for these systems is an increased amount of signal and/or integration time, allowing many photo-electrons to interact with the sensor.

B. Field Performance Prediction: Two models have been used for performance prediction: the ACQUIRE metric and the TTP metric. **Figure 3** describes how field performance is predicted. A target is characterized based on its dimension (the square root of target area) in meters, source contrast, and its task discrimination difficulty (N50 or V50). Contrast is affected by the atmosphere, with an apparent contrast visible at the sensor. The intersection of the apparent target contrast and the sensor CTF describes the highest frequency that the sensor can resolve at that particular contrast, and is referred to as the “limiting frequency.” In the ACQUIRE metric the limiting frequency, in cycles per miliradian, is converted to “cycles on target” by multiplying it by the target angular subtense, which is the characteristic dimension divided by range. This can then be compared to the discrimination criteria (N50), sometimes called the Johnson criteria, to determine probability. The N50 is the number of optical cycles required to achieve a 50% likelihood of target discrimination, is different for detection, recognition, and identification and determined experimentally. The ratio of cycles on target to N50 is input to the target transfer probability function (TTPF) to provide a probability. This process is repeated at various ranges and the probability is plotted as a function of range.

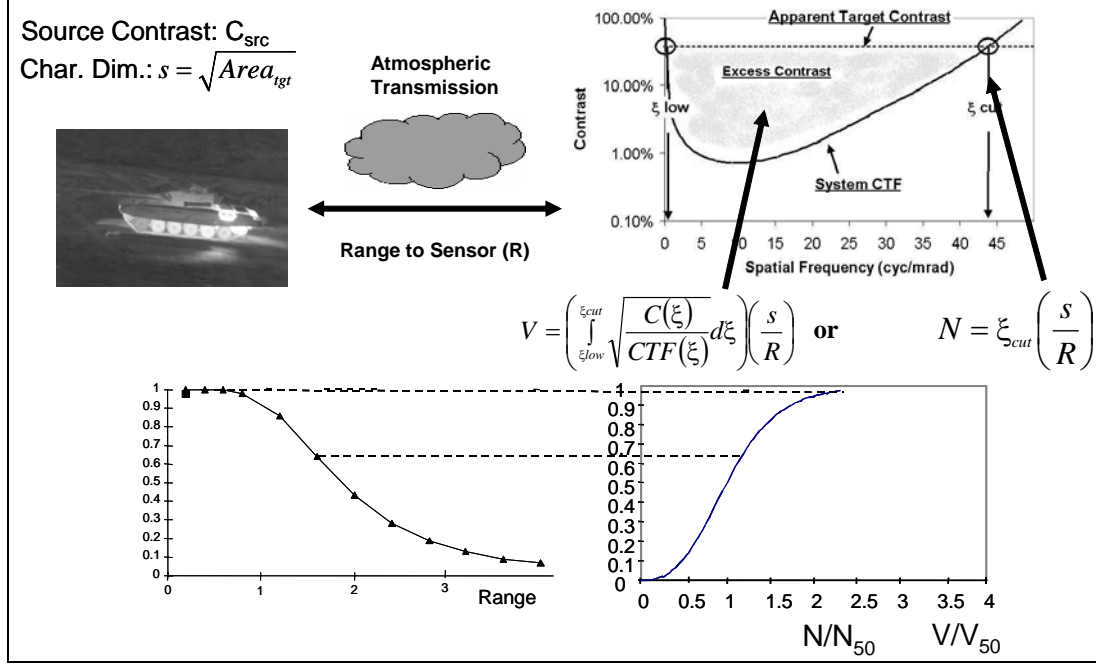


Figure 3. The ACQUIRE and TTP model process

The TTP model [37] has largely replaced the ACQUIRE model and was developed to account for the systems resolution and sensitivity by integrating the system CTF, as shown in **Equation 2**.

$$V = \int_{\xi_{low}}^{\xi_{lim}} \sqrt{\frac{C_{tgt}}{CTF_{sys}(\xi)}} d\xi \quad [\text{cycles}] \quad (2)$$

In this approach the amount of excess contrast that the human eye can see is given weight by taking the ratio of the target contrast to the system CTF. This makes the TTP metric sensitive to image qualities that the ACQUIRE metric is unable to quantify. The beginning and ending intersects of the apparent target contrast with the system CTF provide the limits. Both the horizontal CTF and vertical CTF are assessed separately, and the geometric mean is taken of the results. The results are then compared to the discrimination criteria (V50) to determine the probability. TTPF is again used for the ratio of V to V50 to assess the probability of task performance, though it is different than that used in the ACQUIRE process. TTPF is derived from **Equation 3**:

$$P = \frac{\left(\frac{N}{N50}\right)^\beta}{1 + \left(\frac{N}{N50}\right)^\beta} \quad (\text{ACQUIRE}) \quad \text{or} \quad P = \frac{\left(\frac{V}{V50}\right)^\beta}{1 + \left(\frac{V}{V50}\right)^\beta} \quad (\text{TTP}) \quad (3)$$

The coefficient, β , for the TTP is $1.51+0.24(V/V50)$. The coefficient for ACQUIRE traditionally is $2.7+0.7(N/N50)$, but a single coefficient value of 3.8 gives very close results. The traditional ACQUIRE coefficient has been used in many sensor specifications and combat simulations, however, a great deal of real field data has been shown to match a more gradual probability curve with coefficient equal to $1.75+0.35(N/N50)$ or a single coefficient of 2.7.

The TTP process provides a much more accurate prediction of field performance than the ACQUIRE process as has been demonstrated in numerous recognition and identification experiments. [38] It is able to predict the impact on sensor performance of colored noise and frequency boost, and does an excellent job of performance prediction in both well-sampled and under-sampled images.

When performing the search and detection process, the difficulty in detecting the target is highly dependent on target contrast and the competing clutter level. ACQUIRE-LC [39] was developed to predict detection probability against camouflaged targets, but has been recently modified to work against conventional targets.

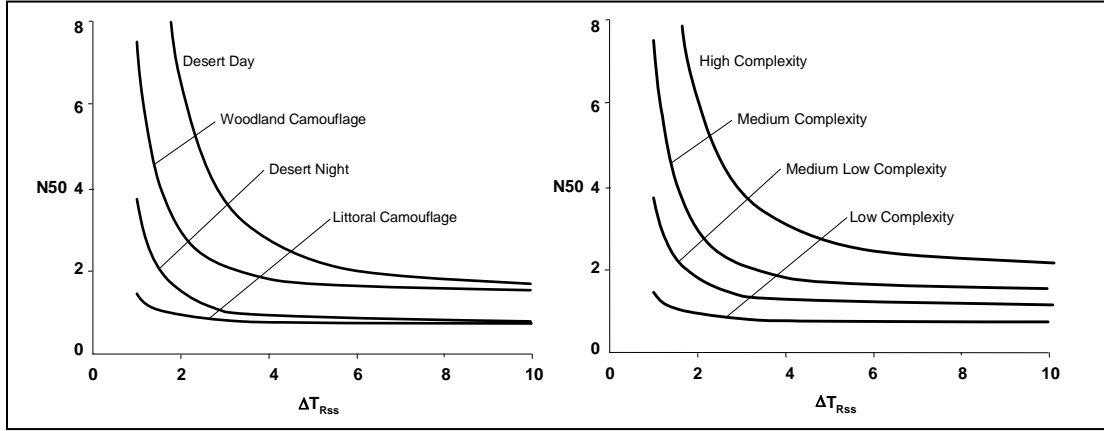


Figure 4. ACQUIRE-LC (left) and Detect05 (right) (ΔT_{RSS} in Kelvin).

The N50 required for the detection of a target in various backgrounds (and clutter levels) is shown, left side of **Figure 3**, as a function of target contrast (RSS) differential temperature in Kelvin [39] and for different background environments. The ACQUIRE-LC equation is

$$N50 = \frac{6}{\Delta T_{RSS}} + 1.5 \text{ (woodland)} \quad N50 = \frac{0.75}{\Delta T_{RSS}} + 0.75 \text{ (littoral)} \quad (4)$$

The N50 is the number of cycles on target required for a 50 percent probability of detection. This N50 is used in the ACQUIRE process described in the previous section to convert sensor CTF and the target detection task into a probability of detection as a function of range.

The ACQUIRE-LC curve is really a signal-to-clutter detection model, where the performance of a human/sensor pair can be characterized as a function of “complexity,” which might be a soft term for clutter. The Detect05 curve is on the right in **Figure 4** and the equation is a single equation

$$N50 = 0.75C \left[\left(\frac{C}{\Delta T_{RSS}} \right)^2 + 1 \right] \quad (5)$$

where C is the complexity. C is 1, 1.5, 2.0, and 2.7 for low, medium-low, medium, and high complexities, respectively. **Figure 5** shows some examples of complexity background levels.

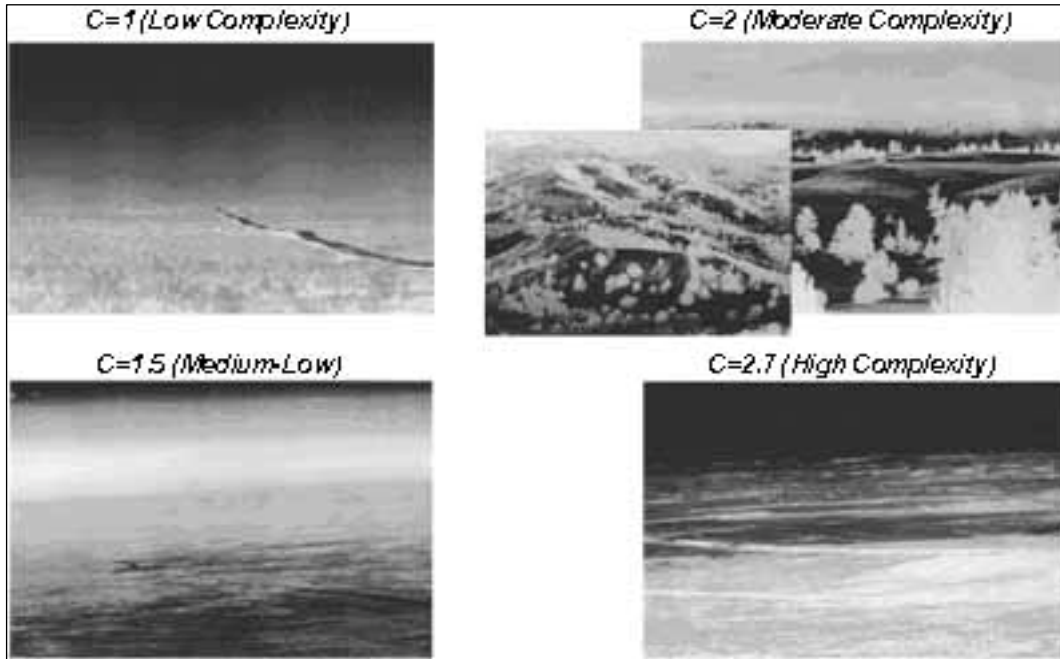


Figure 5. Clutter complexity levels

The models presented so far allow for the ACQUIRE process implementation of both ACQUIRE-LC and Detect05, but implementation in the TTP process requires the relationship between V50 and N50 (note: It is the intention of the Army modeling community to transition from ACQUIRE-LC to Detect05 for both low contrast and conventional targets and for both sensor design and combat simulations). For either curve, the relationship between V50 and N50 is

$$V50 = 4.0N50 + 2.0. \quad (6)$$

This equation allows the implementation of either ACQUIRE-LC or Detect05 in the TTP process as demonstrated in **Figure 6**.

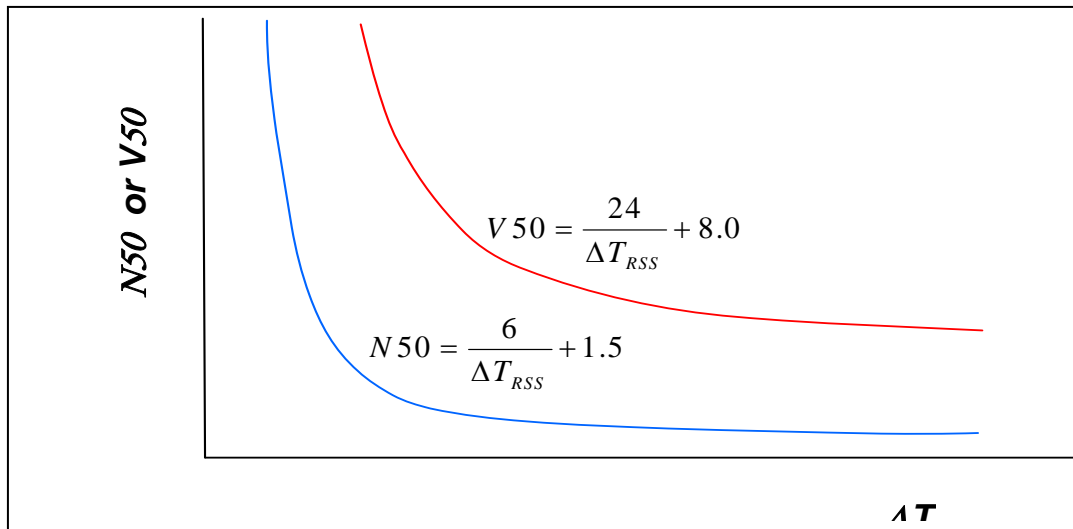


Figure 6. ACQUIRE-LC for Both N50 and V50

5.3. Measurement of Visual Performance

A. The models of predicted performance outlined above predict the quality of a sensor/retinal image and, therefore the probability that an observer can accomplish certain target acquisition tasks at certain ranges. These target acquisition tasks are defined in terms of a hierarchy of discrete “levels” that are detect (D), classify (C), recognize (R), and identify (I). These acquisition tasks and the hierarchy have been defined in an operational context that attempts to provide increasing situational awareness regarding the target or object of interest, and to relate that situational awareness to the contemporary rules of engagement. These definitions also relate to the degree that the observable features allow the observer to discriminate that target from other targets or from background.

Traditionally, the hierarchy and associated task difficulties have been well defined for such military targets as tracked and wheeled combat vehicles. However, recently there has been emphasis placed on defining the relevant observables associated with targets of interest in urban operations, asymmetrical and low-intensity conflicts, and the global war on terrorism. And, only recently has there been a methodical or logical association of these activities and observables with the target acquisition hierarchy. This study will emphasize military tasks/targets expected to be seen in an urban environment that are consistent with the global war on terrorism.

In March 2005, NVESD and TRAC published the report [40] “Acquisition Level Definitions and Observables for Human Targets, Urban Operations, and the Global War on Terrorism”. This report expands upon the acquisition task definitions to add objects of interest in Urban Operations and the Global War on Terrorism to the traditional list of military objects. These definitions follow (note: definitions not related to this proposal were omitted):

Detection. The determination that an object or location in the field of view may be of military interest such that the military observer takes an action to look closer: alters search in progress, changes magnification, selects a different sensor, or cues a different sensor.

Classification. The object is distinguished or discriminated by class, like wheeled or tracked, human or other animal. Possibilities are:

- Tracked vehicle
- Wheeled vehicle
- Humans
- Other animal
- All other non-military inanimate objects

Recognition. For vehicles and weapons platforms, the object can be distinguished by category within a class, such as tank or personnel carrier in the class of tracked vehicles. Examples include, but are not limited to:

- Tracked commercial vehicle – dozer or excavator
- Wheeled military vehicle – air defense or personnel carrier or artillery or tank or utility vehicle
- Wheeled commercial vehicle – heavy transport, light transport, utility vehicle (pick-up or SUV)
- Sedan

For humans, the perception of individual elements, a combination, or a lack of, equipment, hand-held objects, and/or posture that can be distinguished to the extent that the human is determined to be of special military interest. Examples include:

- Wearing head-gear
- Carrying single-hand held object(s)
- Carrying linear two-hand held object
- Wearing “load-bearing equipment”

Identification.

For commercial vehicles, the object is distinguished by typically know model types. Examples include:

- Box truck or single- unit combination (tractor-trailer) or multi-unit combination
- 4-dr sport utility vehicle or 2 door sport utility vehicle or 2 door pick-up
- 4-door sedan, 2-door coupe, 2-door convertible
- Dozer or front-end loader or tractor or “other” agricultural vehicle

For humans, the perception of individual elements or a combination of elements, such as clothing, equipment, hand-held objects, posture, and/or gender that can be distinguished to the extent that the human is determined to be armed or potentially combatant. Examples include:

- Armored head-gear or construction helmet or turban, etc
- Hand-gun or grenade or cell phone
- Rifle or rake or shovel, etc
- Load-bearing equipment or “back-pack” or “nap-sack
- Uniformed infantry or police, or guard or non-uniformed “civilian”

Feature identification.

Commercial vehicles can be distinguished by make and model. Examples include:

- Dodge 4-dr sedan, Audi 2-dr sedan, Porsche 2-dr convertible

Individual elements of clothing, equipment, hand-held objects, and/or gender can be discriminated by name or country/region of origin:

- RPG-7 or AT-4
- M16 or AK-47
- Cell phone or revolver
- Uniform worn by French or US or Chinese infantry
- Facial recognition/identification (A particular person can be discriminated out of a crowd of “n” persons)

The measurement of recognition and identification field performance involves a forced-choice experiment, typically three choices for recognition and twelve choices for identification, where an observer is trained on the targets and is required to decide which target they believe is presented. There are usually ten to twenty observers, around 4 to 6 ranges, and a good assortment of targets and aspect angles. The observer responses are averaged over aspect and target to result in an “ensemble” probability as a function of measured range. *Figure 7* shows average probabilities of actual recognition data as a

function of range on the top left. Since the discrimination task is recognition (3 choices) the guess rate (P_{chance}) is 0.33. The right top graph, in **Figure 7**, shows the data corrected for chance, where

$$P_{correct} = \frac{P - P_{chance}}{1 - P_{chance}} \quad (7)$$

Most military subjects are not experts and train to a proficiency (P_{expert}) of somewhere between 0.9 and 0.95 probability of recognition or identification. Senior enlisted military subjects perform at a much higher proficiency with a P_{expert} of 1.0. The level of proficiency sometimes requires a correction that is described by

$$P_{correct} = \frac{P - P_{chance}}{P_{expert} - P_{chance}} \quad (8)$$

Corrected data (bottom of **Figure 7**) is required for comparison of field performance data with the model predictions. Since, field data is very expensive to acquire, the community would like to use validated model data to supplement field testing to the extent practical.

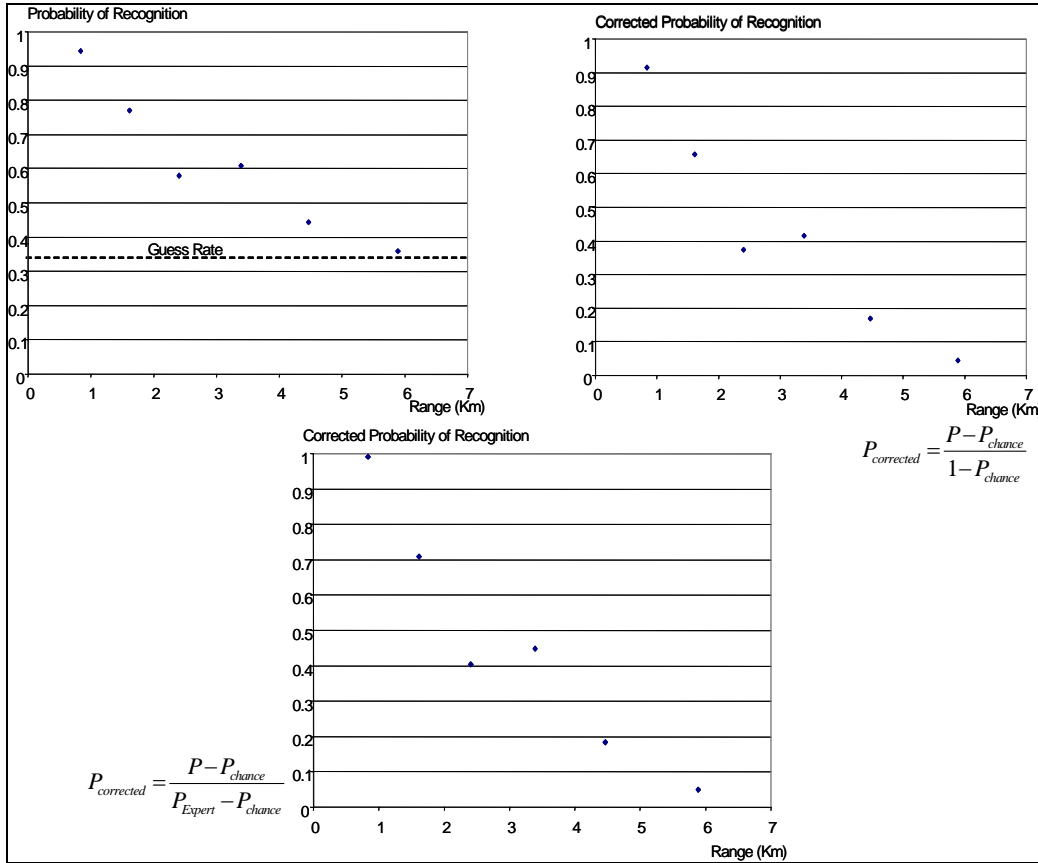


Figure 7. Corrected Field Performance Data (top left is raw data, top right is corrected for chance, bottom is corrected for observer proficiency)

The study will evaluate visual performance in mesopic conditions, and assess if there is a significant difference in performance by observers who have had different types of refractive surgery or if there is a significant difference between predicted performance and actual performance.

6. PLAN

6.1 New Investigational Drugs/ Investigational Devices Exemption Status

None/not applicable. All procedures will be performed on an FDA-approved excimer laser system and post-operative regimen will use commercially available medications and contact lenses.

6.2 Selection of Subjects

6.2.1 Subject Population

A total of 336 myopic active duty U.S. Army patients of both sexes, 21 years of age or older, will be recruited from active duty units stationed in the National Capital Area. We will enroll 224 nearsighted soldiers to WFG photorefractive keratectomy (PRK), WFG LASIK, WFO PRK or WFO LASIK (56 in each group). 112 additional subjects ineligible for LASIK due to thin corneas ($<500\mu$.) will be enrolled in a sub-protocol to receive WFG PRK or WFO PRK (56 in each group). A separate consent form will be provided for both the main group and the subgroup. The military Optometry and/or Ophthalmology clinic will screen potential study candidates referred by the units and those that self-refer by expressing interest in having refractive surgery. The screening providers will refer those who meet all inclusion and exclusion criteria to the Ophthalmology Service at Walter Reed Army Medical Center for enrollment in the study. Each subject will undergo a comprehensive eye examination at Walter Reed. Subjects will be given extensive counseling on the alternative treatments, including risks and benefits of each.

Subjects will provide informed consent to undergo either LASIK or PRK. Participants in the WFO treatment group will all have their eyes treated with the Allegretto Wavelight Excimer Laser System. Participants in the WFG treatment group will have their eyes treated using the VISX Star S4 Excimer Laser System. Laser systems will be operated by qualified clinical investigators from the Walter Reed Army Medical Center Ophthalmology Service. This will include the named investigators for this protocol and other WRAMC ophthalmic surgeons certified for use of the above laser systems in PRK and LASIK

6.2.2. Inclusion and Exclusion Criteria

Each subject must meet all inclusion/exclusion criteria in the treated eye to be considered eligible for enrollment in the study.

Inclusion Criteria:

1. Informed Consent
2. Normal, healthy active adults with access to medical care at Walter Reed Health Care System.
3. Male or female at least 21 years old at the time of the pre-operative examination, and have signed an informed consent. The lower age limit of 21 years is intended to ensure documentation of refractive stability.
4. Myopic spherical manifest refractive error from -1.50D up to -10.00D inclusive, with no more than 4.00D of manifest cylinder refractive error.
5. Inclusion based on pre-op Central Corneal Thickness (CCT) will be assessed according to Residual Stromal Bed Thickness (RSBT) using the following chart (*Table 1*):
6. Patients with CCT <500 will only be able to receive PRK and will be randomized in a separate PRK subgroup.
7. Best spectacle corrected visual acuity (BSCVA) of at least 20/20 in the study eye.
8. Soft contact lens users must have removed their lenses at least two weeks prior to baseline and

follow-up measurements.

9. Hard contact lens users (polymethylmethacrylate (PMMA) or rigid gas permeable lenses) must have removed their lenses at least four weeks prior to baseline and follow-up measurements.

Table 1. Preoperative corneal thickness and manifest refraction matrix to ensure residual stromal bed thickness (RSBT) of at least 300 microns after laser in situ keratomileusis (LASIK).*

Pre-op Pachy - US (microns)	RSBT of 300 microns Max sph + cyl
<500	PRK only, sub-protocol
500	-5.50 D
510	-6.25 D
520	-7.75 D
530	-8.25 D
540	-9.50 D
550	-10.50 D
≥560	all

* Calculated based on 120 micron LASIK flap.

10. Refractive stability must be documented by previous refractions. Spherical and cylindrical portion of the manifest refraction must not have varied by more than 0.50 diopters over the previous 12 months.
11. Exhibits strong motivation for keeping the follow-up visits.
12. Available for evaluation at Walter Reed during the follow-up period.
13. Willing and available to undergo testing at Ft. Belvoir during the study period.
14. Service members must have their command approval to participate in the study.
15. Access to transportation to meet follow-up requirements.

Exclusion criteria:

1. Residual, recurrent or active ocular diseases or corneal abnormalities in either eye such as iritis, uveitis, keratoconjunctivitis sicca, herpetic keratitis, vernal conjunctivitis, lagophthalmos, corneal scarring, anterior basement membrane disease, recurrent erosions, glaucoma, previous steroid responder, occludable chamber angles, visually significant cataracts.
2. History of any previous eye surgery or trauma, including previous refractive surgery.
3. Dry eye as reflected by Schirmer's test, subjective complaints or symptoms of dry eye, findings during slit lamp exam that would be consistent with dry eye (e.g. superficial punctuate keratitis).
4. Corneal thickness insufficient to allow the residual remaining stromal bed to be no less than 300 microns in each eye. The residual stromal bed thickness will be determined by subtracting

both the LASIK flap thickness and depth of the ablation from the total central corneal thickness measured by pachymetry.

5. Female subjects who are pregnant, breast-feeding or intend to become pregnant during the study. This is standard of care exclusion for refractive surgery at the Walter Reed Refractive Surgery Center because of the medications that are routinely given as part of the procedures. Standard of care analgesia consists of medications (e.g. narcotics) labeled as Pregnancy Category “C” by the FDA. Teratogenic effects are not known, however, physical dependence in the neonate may occur if the mother is given narcotics. Female subjects will be given a urine pregnancy test prior to participating in the study to rule out pregnancy.
6. Concurrent topical or systemic medications that may impair healing, including corticosteroids, antimetabolites, isotretinoin (Accutane®), amiodarone hydrochloride (Cordarone®) and/or sumatriptan (Imitrex®) (other medications in the same family as Imitrex will still be allowed).
7. Significant corneal neovascularization.
8. Progressive myopia or keratoconus.
9. Medical condition(s), which, in the judgment of the investigator, may impair healing, including but not limited to: collagen vascular disease, autoimmune disease, immunodeficiency diseases, and ocular herpes zoster or simplex.
10. Patients with known sensitivity or inappropriate responsiveness to any of the medications used in the post-operative course.
11. Any physical or mental impairment which would preclude participation in any of the examinations.

6.2.3 Recruitment

Subjects will be recruited from patients electing to undergo refractive surgery at WRAMC, Center for Refractive Surgery. Patients will be counseled on the risks and benefits of both PRK and LASIK refractive surgery, as well as provided information on the currently available alternatives not included in the study, including LASEK (laser subepithelial keratomileusis), or epi-LASIK (epithelial laser-assisted in situ keratomileusis). Patients who are eligible and interested will be given study information and contact information for the WRAMC Ophthalmology Clinic, which is the office of the PI. Patients who contact the WRAMC Ophthalmology Clinic or Center for Refractive Surgery, 202-782-0202/ 0204 and are eligible for refractive surgery will be provided information on the study.

6.2.4 Consent Process

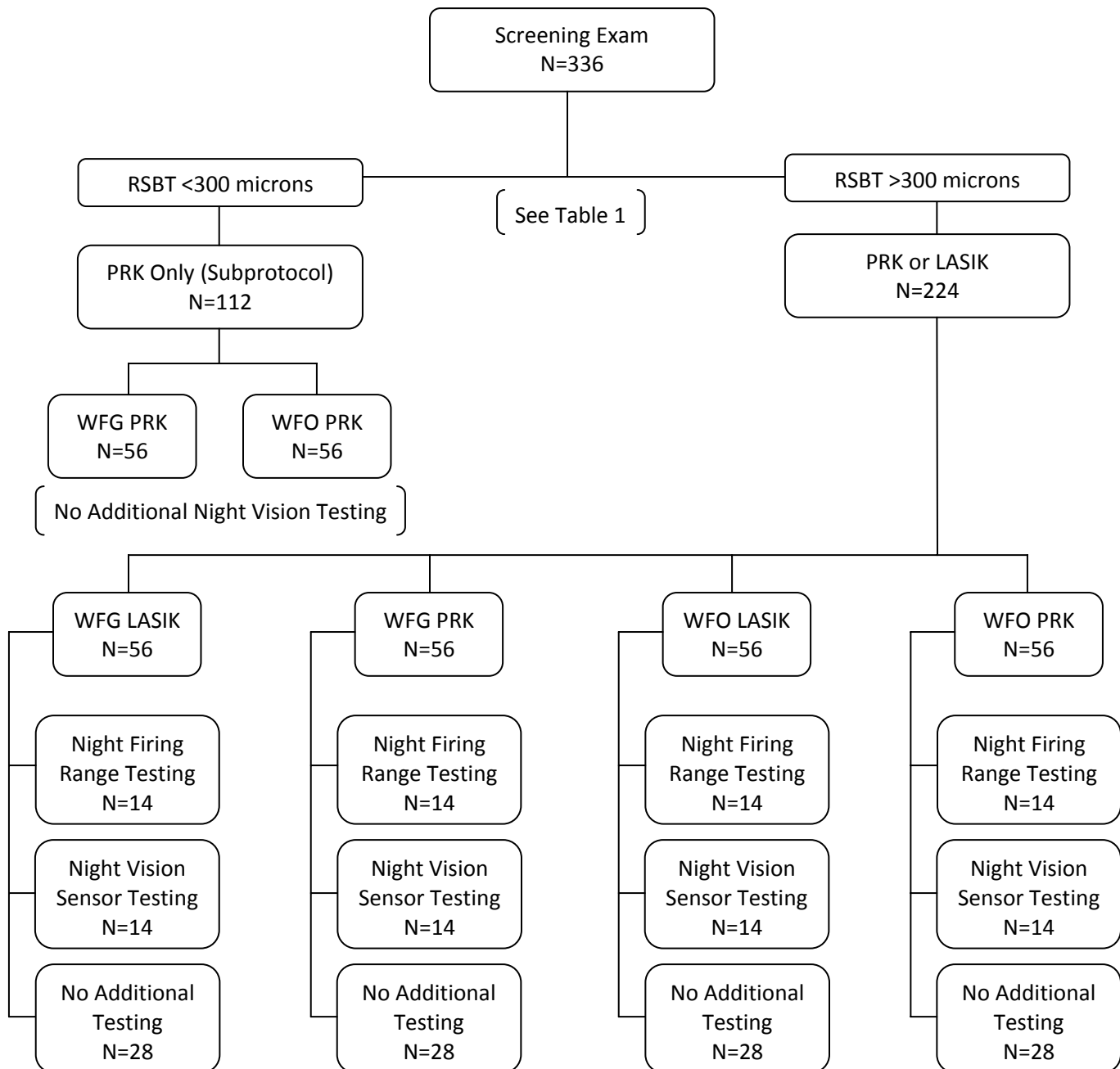
Each participant will provide fully informed consent for participation after extensive counseling on the risks, benefits and alternatives to refractive surgery and their involvement in this study during the screening appointment. Trained members of the research team (Jayson Edwards, Denise Sediq, Lamarr Peppers) will provide all counseling in a private and confidential setting. One room of the laser center is designated specifically for patient counseling. The research team or the principal investigator will answer all questions regarding the surgery itself or any details of the study fully to the patients' satisfaction. The principle investigator and/or associate investigators will present and explain in detail the consent and HIPPA Authorization forms to potential participants. If interested, eligible individuals will be given the opportunity to ask and have all questions answered before signing the informed consent document and HIPPA Authorization form.

6.3 Study Design and Methodology

6.3.1 Study Design: Single-center randomized prospective study

6.3.2 Study Methodology. In this prospective randomized study, a total of 336 patients undergoing

refractive surgery will be recruited consecutively at WRAMC. We will enroll 224 nearsighted soldiers to WFG photorefractive keratectomy (PRK), WFG LASIK, WFO PRK or WFO LASIK (56 in each group). 112 additional subjects ineligible for LASIK due to thin corneas ($<500\mu$,) will be enrolled in a sub-protocol to receive WFG PRK or WFO PRK (56 in each group). (See page 27, Sample Size Estimation, Randomization, 3rd paragraph). All qualified patients who meet the enrollment criteria (see above) will be invited to participate in the study. Those patients who meet the above criteria and volunteer to participate, after signing the written informed consent, will undergo either WFG PRK, WFG LASIK, WFO PRK or WFO LASIK by a qualified refractive surgeon. Subjects will be randomized using a computer program based on random number generation, with an equal number of subjects in each group.



WFO ablations will be done using the Allegretto Wavelight Excimer Laser System. WFG ablations will be done using the VISX S4 Excimer Laser System. All clinical measurements will be done at the WRAMC Center for Refractive Surgery. Subjective analysis of contrast sensitivity will be evaluated using the Cambridge Research Systems Visual Stimulus Generator. Objective analysis of optical quality will be assessed using a Hartmann-Shack wavefront aberrometer. Military performance evaluation of night vision and contrast sensitivity will be assessed using target detection and identification tests as well as the night firing range in collaboration with the U.S. Army Night Vision Laboratory, Ft. Belvoir, VA. Subjects will be trained in night vision goggle use if elected to undergo night vision testing. All testing will be done in a before-after design. Patients and evaluating opticians will be masked as to whether wavefront was guided or optimized. Due to the difference in surgical techniques between LASIK AND PRK, it is not possible to mask either the patient or evaluating optician. Pre-operative measures will consist of a one time only measure of the key variables, while post-operative measures will consist of 2 evaluations of the same variables made at 6 weeks and 6 months following the procedure. All patients will be informed of possible additional testing done at Ft. Belvoir, and randomization done during screening to determine what, if any, additional testing be done. Subjects will be made aware that the study requires travel to Ft. Belvoir which the service members will arrange themselves and fully evaluated to assure that they will be willing to participate with these additional requirements.

Clinical Examination Specifics

1. **Psychometric questionnaire [SOC]** will be given at the beginning of the examination with sufficient time allotted to ensure completion. The questionnaire assesses subjective quality of vision (glare, halos, night vision, etc.). The questionnaire will be self-administered and reviewed for completion before the examination is complete.
2. **Pupil size [SOC]** will be measured during preoperative examination under dim light (<5 lux, 0.1cd/m²) with the patient fixating on a distant image. The measurement will be taken with the Colvard pupillometer or equivalent device.
3. **Biomicroscopic examination [SOC]** will evaluate the lids, conjunctiva, sclera, surface integrity and tear stability, cornea, anterior chamber, and iris.
4. **Corneal haze [SOC]** will be subjectively evaluated by biomicroscopic examination and graded on a standard five-point scale (clear (0), trace (1), mild (2), moderate (3), or severe (4)).
5. **Manifest refraction [SOC]** will be obtained by a fogged "push plus" technique using a standardized phoropter with a vertex distance of 12.5mm.
6. **Uncorrected (UCVA) and best-corrected visual acuity (BCVA) [SOC]** (distance) will be evaluated with a 4 meter logMAR back-illuminated eye chart (Lighthouse Second edition, New York, NY). Room illumination will be standardized and verified with a hand held meter for all acuity measurements. BCVA will be tested with the subject viewing through a phoropter. Acuity measurements will be recorded as the Snellen equivalent. At least 3 letters must be correctly identified to score a line. The number of letters missed or the number of letters correctly identified in the next line will be recorded; i.e. 20/25-2 indicates that the subject correctly identified 3 of 5 letters on the 20/25 line.
7. **Keratometry [SOC]** will be assessed with either a manual or auto-keratometer.
8. **Corneal topography [SOC]** will be recorded with a computerized videokeratography (Humphrey or similar) according to manufacturer instructions.
9. **Intraocular pressure (IOP) [SOC]** will be measured by applanation tonometry.

10. **Contrast sensitivity [SOC]** will be measured under photopic, mesopic and night vision conditions. Photopic testing will be conducted with a back-illuminated chart (5% Contrast Acuity test, or similar). Mesopic testing will be conducted with a back-illuminated chart (25% Contrast Acuity test, or similar) and neutral density filter. Night vision testing will be conducted with a back-illuminated chart (25% Contrast Acuity test, or similar) and green night vision filter. All examinations will be conducted with the room lights turned off under best-corrected vision with the use of a phoropter or trial frames.
11. **Cycloplegic refraction [SOC]** will be performed 30 minutes after 2 doses of 1% mydriacyl using a standardized phoropter and a vertex distance of 12.5mm.
12. **Posterior ocular examination [SOC]** will be conducted using the biomicroscope with a neutralizing lens and indirect ophthalmoscopy. The crystalline lens, vitreous, optic nerve, macula, retinal vessels, and peripheral retina will be examined.
13. **Corneal thickness [SOC]** will be conducted with an ultrasound pachymeter on the central cornea.
14. **Wavefront measurement [EXP]** will be taken with the COAS™ (Complete Ophthalmic Analysis System™) wavefront analyzer (Wavefront Sciences, Albuquerque, NM) before and after cycloplegia according to manufacturer's instructions. For the pre-operative examination, the pupil must be at least 7-mm in each of five image captures for each eye. For post-operative examinations, every effort will be made to capture three images per eye with a 7-mm minimum pupil diameter.
15. **Contrast Sensitivity Function (CSF) [EXP]** will be assessed using the Cambridge Research Systems Visual Stimulus Generator (Rochester, England). This instrument displays calibrated visual stimuli on a CRT-based computer monitor for precise amounts of time. Stimuli are horizontal sinusoidal grating patterns with variable spatial frequencies. The observer's task is to press one of two buttons to indicate the presence and location of the stimuli on the screen. A plot of contrast sensitivity versus spatial frequency generates the contrast sensitivity function.
16. **Super Vision Test [EXP]** was developed by Dr. Jeff Rabin and provides both visual acuity and contrast sensitivity on a single chart. High contrast visual acuity ranges from 20/32 to 20/5. Small letter contrast sensitivity is 20/25 with a spatial frequency of 24 cycles/degree at 4 meters.

Military Task Performance Examination Specifics

1. **Visual Performance Predication Modeling [EXP].** Target Task Performance [TTP] will be performed on all subjects to analyze data derived from the contrast sensitivity function.
2. **Threshold target identification [EXP].** 56 Subjects will be randomly selected (14 WFO PRK, 14 WFO LASIK, 14 WFG PRK, and 14 WFG LASIK) to perform this task. Subjects tested with a 12 alternative forced choice paradigm. The targets will be tracked vehicles and will be presented to the observers on a monitor at a sufficient distance to stress the eye response. The percentage of correctly identified stimuli will then be plotted as a function of range to produce a psychometric function. Outcome measure of threshold target identification at a certain range/distance will be compared pre-operatively and post-operatively.
3. **Night firing range [EXP].** 56 different subjects (14 WFO PRK, 14 WFO LASIK, 14 WFG PRK, and 14 WFG LASIK) who did not participate in the Threshold testing above will be randomly selected and tested at the NVESD night firing range. Testing and training will be conducted under strict supervision in the Night Vision Tunnel that is routinely used for firing to

evaluate sights. Subjects will fire the M16A2 using only their dominant eye (corrected and uncorrected) under the following conditions: 1) night vision goggle and aiming light; 2) gun-mounted thermal sight; and 3) iron sight. Light levels for conditions 1 and 2 will be starlight only and for condition 3, low light (simulated dusk). Outcomes measurements will be accuracy (average distance from target center) and precision (standard deviation of distance to target). Comparison will be made pre and post surgery.

Surgical Procedure (PRK & LASIK) [SOC]:

Each surgeon will be trained, experienced and certified to use the surgical equipment. Wavefront optimized PRK and LASIK treatments will be performed with the Allegretto Wavelight excimer laser system (Alcon Surgical, Fort Worth, Texas) at the Center for Refractive Surgery, Walter Reed Army Medical Center. Wavefront guided PRK and LASIK treatments will be performed using the VISX Star S4 WFG excimer laser (Advanced Medical Optics, Santa Ana, California) at the Center for Refractive Surgery, Walter Reed Army Medical Center. .

The manufacturer's recommended guidelines will be observed to ensure safety, proper calibration, treatment data entry, focus, alignment, and laser operation. Trained ophthalmic technicians will perform all of the duties of the operating technician, including calibration. Environmental conditions will be adjusted, monitored, and recorded to standardize the surgical protocol. Every effort will be made to conduct treatments between 30% and 60% relative humidity and 68 to 72 degrees Fahrenheit (20-22 degrees Celsius).

Patients will be brought into the laser suite and positioned under the laser. Proparacaine 0.5% ophthalmic solution hydrochloride will be administered in the inferior fornix for topical anesthesia. The eyelids will be draped with adhesive plastic drapes, and gently retracted with a wire eyelid speculum. The operative eye will be aligned with the laser system centered on the entrance pupil and the eye tracking system engaged according to the manufacturer's guidelines prior to removing the epithelium (PRK), or cutting the flap (LASIK).

Both WFG (VISX) and WFO (Allegretto) ablation patterns will be programmed using a 6.5mm optical zone with a transition zone extending to 8 mm. Eyes must have sufficient corneal thickness to allow the residual remaining corneal stromal bed to be no less than 280 microns. The residual stromal bed thickness will be estimated by subtracting both the LASIK flap thickness and estimated depth of the ablation from the total central corneal thickness.

Photorefractive keratectomy (PRK). All PRK patients will have epithelium removed using a rotary brush (Amoils Epithelial Scrubber, Innovative Excimer Solutions, Toronto, Canada). After ensuring proper patient fixation, engagement of the eye tracking system, and alignment of the reticles, the laser treatment will be performed. Following laser ablation, the cornea will be immediately irrigated with chilled balanced salt solution. Prophylactic mitomycin-C (MMC) will be used on all PRK eyes with central ablation depth of greater than 75 microns. A corneal light shield soaked in 0.2 mg/ml (0.02%) MMC solution will be placed over the central cornea for 30 seconds after laser ablation. The MMC will then be irrigated from the ocular surface with 30 ml of balanced saline solution. Topical antibiotic, steroid and non-steroidal eye drops will be administered and a bandage contact lens placed over the cornea. The contact lens will be left in place until complete re-epithelialization, in most cases by post-op day 3 or 4.

Laser-assisted in-situ keratomileusis (LASIK). After topical anesthesia and surgical prep similar to PRK, all LASIK patients will have superior-hinged lamellar flaps created with the Intralase femtosecond laser keratome (AMO Surgical, Irvine, CA). The Intralase laser will be programmed to create a flap of 9.0 mm or greater at a target depth of 120 microns. After ensuring proper patient fixation, engagement of the

eye tracking system, and alignment of the reticles, the laser treatment will be performed. Following laser ablation the flap will be carefully returned to its original position and the surgeon will irrigate under the flap with BSS. Topical antibiotic, steroid and non-steroidal drops will be administered at the conclusion of the case.

Postoperative Medications/Regiment [SOC]

The following medication regimen will be prescribed:

1. **Systemic analgesics [all patients]:** Ibuprofen 800 mg po every 8 hours as needed for pain, and/or Percocet (Endo pharmaceuticals, Chadds Ford, Pennsylvania) 1-2 tablets every 4-6 hours as needed for pain.
2. **Topical antibiotic [all patients]:** Topical moxifloxacin (Vigamox®, Alcon Laboratories, Ft. Worth, Texas) or gatifloxacin (Zymar®, Allergan, Inc., Irvine, California) will be administered four times per day for one week postoperatively or until the epithelium is closed then discontinued.
3. **Topical steroid [PRK patients]:** Fluoromethalone 0.1% ophthalmic solution 4 times a day for the 4 weeks, then 3 times a day for the next two weeks, twice a day for next two weeks, then once a day for two weeks.
4. **Topical steroid [LASIK patients]:** Prednisolone acetate 1.0% ophthalmic suspension 4 times a day for 1 week.
5. **Topical analgesic [all patients]:** Ketorolac tromethamine 0.5% preservative free (Acular PF®, Allergan, Inc., Irvine, California) administered no more than four times daily as needed for pain in the first 24 hours after LASIK and up to 72 hours after PRK.
6. **Non-preserved artificial tears [all patients]:** One drop 4 times a day placed into the inferior cul-de-sac for two weeks and then as needed.

Retreatment [SOC]

The minimum time for retreatment (enhancement) is 6 months. To qualify, eyes must have an UCVA worse than 20/20, at least 0.50D residual refractive error (sphere and/or cylinder), no significant loss of BSCVA (≤ 2 lines), and stable refractive error defined as no more than 1.00D change in either sphere or cylinder over at least a 3 month period.

Retreatment will be the same procedure as original treatment. Examination follow-up schedule for retreated eyes will be the same as primary treatments. The results following retreatment will be analyzed and reported as a separate sub-group.

6.3.3 Collection of the Human Biological Specimens. Not applicable/none.

6.3.4 Data Collection

Demographic (age and sex) and clinical data will be entered directly from the medical record into a Microsoft Excel database. This database will be password protected on a computer in the WRAMC Center for Refractive Surgery. Only the patient's study ID number, and no personal history information, will be used in the data spreadsheet. Only members of the research team listed above will have access to this database. Queries generated from database review will be resolved by reference to the medical record. Entries and necessary changes to the database will be made and electronic audit trails kept in accordance with 21 CFR Part 11.

6.3.5 Study Time Line

Clinical examinations and contrast testing will be done at the WRAMC Center for refractive Surgery. All night vision task performance measurements and firing range performance will be done at the Night Vision Lab at Fort Belvoir, VA. A summary of examinations and testing at WRAMC and NVESD are presented in *Tables 2 and 3*, respectively.

Table 2. Baseline and post-operative clinical examinations and testing.

Clinical Examinations (WRAMC)	Pre-Op	Day 1	Day 3/4	1 Wk	1 Mo	3 Mo	6 & 12 Mo
Medical and ocular history	X						
Contact lens history	X						
Systemic and topical medications	X	O	O	O	O	O	O
Pupil size	X						
Biomicroscopic examination	X	O	O	O	O	O	O
Corneal clarity	X	O	O	O	O	O	O
Manifest refraction	X				O	O	O
Uncorrected distant visual acuity	X	O	O	O	O	O	O
Best corrected visual acuity	X				O	O	O
Keratometry	X				O	O	O
Corneal topography	X				O	O	O
Intraocular pressure	X				O	O	O
Corneal thickness	X						
Contrast sensitivity (photopic)	X				O	O	O
Contrast sensitivity (mesopic)	X				O	O	O
Wavefront measurement (undilated)	X				O	O	O
Cycloplegic refraction	X						O
Wavefront measurement (dilated)	X				O		O
Posterior ocular examination	X						O
Psychometric questionnaire	X				O	O	O
Contrast Sensitivity Function	X				O	O	O
Super Vision Test	X				O	O	O
Assess complications / AEs		O	O	O	O	O	O

X = both eyes O = operated eyes only

Table 3. Baseline and post-operative military task performance testing.

Night Vision Examinations (NVESD, Ft. Belvoir)	Pre-Op	6 Weeks	6 Months
Target Task Performance (Detection and Identification)	X	X	X
Firing Range	X	X	X

6.4 Statistical Consideration

6.4.1 Primary Outcome Measure(s)

- Subjective best focus: UCVA, MR, BSCVA

6.4.2 Secondary Outcome Measure(s)

- Objective optical quality (wavefront aberrometry)
- Contrast threshold function
- Target Task Performance (TTP) metric
- Threshold target identification
- Night firing range scores

6.4.3. Data analysis

Subjective best focus. Refractive surgery outcomes will be evaluated based on accuracy/precision of mean spherical equivalent and accuracy/precision of astigmatic correction as defined by the power vectors J0 and J45.

Objective analysis of optical quality. Postoperative outcomes will be assessed using the Contrast Sensitivity Function, Modulation Transfer Function, Optical Transfer Function, Total RMS, Magnitude of Spherical Equivalent and Magnitude of Coma.

A multi-way (main effects of surgery (LASIK vs. PRK) and wavefront protocols (guided vs. optimized)), repeated measures analysis of variance (ANOVA) will be used to compare visual outcomes between the treatment groups over time.

Contrast Threshold Function will also be measured in two ways:

1. The Contrast Sensitivity Function (measurement is unitless) will be measured at baseline, at 1 month, 3 months, 6 months and 1 year postop. The inverse of this variable is one measure of the CTF.
2. The CTF calculated from the target task performance (TTP) models used by the NVESD.

Agreement between the CTF (calculated from the CSF) and the TTP CTF will be examined using an interclass correlation coefficient and a Bland Altman plot.

Using the CTF calculated from the CSF, the effect of surgery (LASIK vs. PRK) and wavefront protocols (guided vs. optimized) on CSF will be examined using repeated measures analysis of variance.

Objective performance predictions:

Performance prediction before and after surgery will be examined using a multi-way, repeated measures analysis of variance (ANOVA) to compare the treatment groups over time.

The secondary response variable is the score from the night vision firing. The effect of surgery (LASIK vs. PRK) and wavefront protocols (guided vs. optimized) on CSF will be examined using repeated measures analysis of variance, with the additional within subject factor, firing sight (night vision goggles, thermal sight, iron sight).

Sample Size Estimation

AULCTF (area under log of contrast threshold function): The AULCSF is used in sample size estimation because there is existing data for this measure (which is just the inverse of the AULCTF). In a previous study by Sakata et al (2007) the change in AULCSF before PRK was (mean \pm SD, 2.16 ± 0.04) and after PRK (2.02 ± 0.12). The mean change was 0.14 (SD estimated to be 0.15). For the AULCSF calculated from the TTP metric, the sample is limited to 12 subjects per group. Controlling the probability of a Type I error at $\alpha = 0.017$, a sample of 12 subjects per group (i.e. wavefront guided vs. optimization within one type of surgery) would have 80% power to detect a large difference in the change in AULCSF (difference = 0.22), and if there is no interaction, a sample of 23 subjects per group would have 80% power to detect a difference of 0.15 (i.e. a one standard deviation difference).

For the AULCSF calculated the CRS Visual Stimulus Generator, controlling the probability of a Type I error at $\alpha = 0.017$, the following sample sizes will have 80% power to detect the following differences in the changes in AULCSF:

Difference of	N= per group
0.15	23
0.14	26
0.13	30
0.12	34
0.11	41
0.10	49
0.09	60
0.08	75
0.07	98

To power the study to detect a difference of 0.10 between wavefront modalities within a surgical group, we would need 49 subjects per group to complete the study. Using the combined wavefront guided and optimized groups, the study can detect a difference of 0.07 in the change in AULCSF. Therefore, we would request up to 224 subjects to allow for a 10% dropout rate.

NIGHT FIRING RANGE SCORES: Based on a previous study of night vision scores for subjects undergoing PRK vs. LASIK, the mean night firing range scores with iron sights were 97.5 ± 3.1 in the PRK group and 93.7 ± 5.8 in the LASIK group. Controlling the probability of a Type I error at $\alpha = 0.017$ (the alpha is reduced from the usual 0.05 level to account for 3 primary outcome variables using a Bonferroni correction of $0.05/3=0.017$), a sample of 12 subjects per group (wavefront guided and wavefront optimized) within each type of surgery (PRK and LASIK) will have 80% power to detect a difference of 7 in the night firing range scores. In the previous study, there was no significant difference in the night firing range scores between PRK and LASIK, and if there is no interaction (i.e. wavefront guided is only helpful with one type of surgery) then the main effect of wavefront (guided vs. optimized) would include 24 subjects per group. With 20 total subjects per wavefront group, the study would have 80% power ($\alpha = 0.017$) to detect a difference of 5 in the night firing range scores.

Given that the night firing range scores average in the range of 90-98, a difference of 5-7 is less than a 6-8% change in scores, and we would consider this a minimal clinically significant difference to detect.

Randomization

Up to 224 subjects will initially be randomized to one of 12 groups with an equal number of subjects in each group:

1. PRK, Wavefront Guided, Firing range n=12 (up to 14)
2. PRK, Wavefront Guided, Night vision performance testing, n=12 (up to 14)
3. PRK, Wavefront Guided, No additional testing n=24 (up to 28)
4. PRK, Wavefront Optimized, Firing range n=12 (up to 14)
5. PRK, Wavefront Optimized, Night vision performance testing, n=12 (up to 14)
6. PRK, Wavefront Optimized, No additional testing n=24 (up to 28)
7. LASIK, Wavefront Guided, Firing range n=12 (up to 14)
8. LASIK, Wavefront Guided, Night vision performance testing, n=12 (up to 14)
9. LASIK, Wavefront Guided, No additional testing n=24 (up to 28)
10. LASIK, Wavefront Optimized, Firing range n=12 (up to 14)
11. LASIK, Wavefront Optimized, Night vision performance testing, n=12 (up to 14)
12. LASIK, Wavefront Optimized, No additional testing n=24 (up to 28)

Randomization will be determined using a computer program based on random number generation. Patients will be randomized in blocks of 16 subjects (16 instead of 12 because there are 2 'no additional testing subjects' for each 'testing' subject) to ensure that the work load at the Night Vision facility is evenly distributed through the study. Similarly the order of testing at the Night Vision facility will be randomized using a computer program based on random number generation.

Due to budget limitations and scheduling concerns, patients undergoing additional testing at Ft. Belvoir will be selected first and randomized into their respective groups. Two separate randomization schedules will be set up, with those undergoing night vision testing randomized to 8 groups with a total of 112 subjects. The following patients will not undergo night vision testing and will be randomized to 4 groups of 112 subjects.

For the group of subjects with corneal thickness <500 microns, a subgroup with a sample size of 49 subjects per wavefront group would be required to detect a difference of 0.10. No patients in this subgroup will undergo additional night vision testing and will be randomized to either Wavefront Guided or Wavefront Optimized treatments. To allow for dropouts up to 112 subjects would be required for the study.

6.5 Reporting Adverse Events

6.5.1 Expected Adverse Events from Research Risks and Reporting

There are no significant risks that may develop as a result of participation in this study, other than those associated with the procedure itself. None of the testing procedures pose any risk beyond a normal eye examination.

The following are possible risks or discomforts that may develop as a result of undergoing PRK surgery:

- a. Eye discomfort or pain immediately after the procedure. Mild to severe discomfort in the treated eye for several days is common. Eye drops, bandage contact lenses, and oral analgesics are routinely used in the post-operative period to manage pain. In addition, eye patches or other measures may be required during this convalescent period.
- b. Decrease in best-corrected visual acuity (vision with eyeglasses or contact lenses). This complication may occur after up to 7% of treatments. This may improve with treatment. Vision may be treated with glasses post-operatively. Alternatively, contact lenses may be required to improve best-corrected visual acuity. The worst-case would be an inability to correct the visual acuity.
- c. Improper correction. Under-correction (nearsightedness) or over-correction (farsightedness) may occur requiring the use of corrective lenses. There is approximately a 4% chance that you will not achieve 20/40 vision without glasses or contact lenses. You may need to wear glasses or contact lenses after the procedure to attain best vision. Retreatment with another laser procedure may be an option.
- c. Dry eye. Grittiness, scratchiness, foreign body sensation, and fluctuating vision, and sensitivity to dust and smoke are very common in the first 1 to 3 months following surgery. These gradually resolve in the large majority of patients. Up to 5% of patients may have more severe dry eye symptoms that last for a longer period of time. This may require frequent use of lubricant eye drops or other medications to treat the symptoms.
- d. Induced astigmatism. Distortion of vision may require corrective lenses (up to 3%).
- e. Glare and halo from bright lights or halos around lights, especially at night. The glare may be severe enough to cause difficulty driving at night. This usually occurs immediately after the procedure and resolves spontaneously, but may be permanent in approximately 5% of people.
- f. Decrease in contrast sensitivity. This typically occurs immediately after the procedure and usually resolves spontaneously, but may be permanent (up to 3%).
- g. Double vision experienced in one eye. This may occur immediately after the procedure and usually resolves spontaneously as the eye heals. Treatment may be necessary, including corrective lenses or retreatment.
- h. Corneal scarring. Following treatment, your cornea may heal with a scar dense enough to affect the vision (less than 2%). The scar may respond to treatment with medications, but may be permanent and require further surgery, including corneal transplant.
- i. Elevated intraocular pressure. High pressure in the eye may occur while taking eye drops after the procedure (up to 10%). This High pressure usually responds to treatment with topical glaucoma medications.
- j. Recurrent erosions. The corneal epithelium may break down resulting in a painful abrasion. This is treated with topical lubrication and antibiotic medications and may require a therapeutic contact lens (up to 3%).

- k. Microbial keratitis (infection of the cornea) may lead to severe eye damage and loss of vision. Intensive antibiotic therapy is usually required, and surgery may be necessary, including corneal transplant. This complication occurs in less than 0.1% (less than one in one thousand).
- l. Endophthalmitis. A serious and vision threatening infection of the inner tissues of the eye that requires surgery and intensive antibiotics for treatment. Permanent vision loss may result. This complication occurs in less than 0.01% (less than one in ten thousand).
- m. Cataract. Cloudiness of the lens inside the eye, which may reduce vision and require surgery for treatment. (less than 0.1%)

In addition to the above, the following are possible risks or discomforts that may develop as a result of undergoing LASIK surgery:

- n. Flap complications. These occur only with LASIK and may happen at the time of surgery or in the period following the surgery. During surgery, the flap may be cut too thin, incompletely, irregularly, or off-center. These complications may result in irregular healing and loss of vision. In the period following surgery the flap may be dislodged with minor trauma or develop wrinkles (called “striae”), inflammation or debris material under the flap.

The only additional potential risk is in the night firing range. As soldiers, our subjects are all familiar and often expert with weapons and weapon safety, and this risk should be no more than what soldiers undertake every day as part of their training and duty performance. Night firing range testing and training will be conducted under strict supervision in the Night Vision Tunnel that is routinely used for firing to evaluate sights. Strict firing range safety protocols will be followed at all times to ensure safety of the participants and range staff.

6.5.2 Reporting Serious and Unexpected Adverse Events to the IRB

The principal investigator (PI) within one working day must report all serious adverse events occurring in subjects enrolled at WRAMC to the Human Use Committee (HUC). This is accomplished by submitting an adverse event report memorandum to the HUC via DCI.

Serious adverse events must be reported even if the PI believes that the adverse events are unrelated to the protocol.

Unexpected (but not serious) adverse events occurring in subjects enrolled at WRAMC which, in the opinion of the PI, are possibly related to participation in the protocol must be reported by the PI within 10 (ten) working days to the HUC using the same procedure.

For all serious and/or unexpected adverse events, the PI must forward a copy of the adverse event report to the Medical Monitor for the protocol.

Expected adverse events, (i.e., those events included as potential risks in the consent form) which are not serious, should be reported yearly on the Annual Progress Report (APR) for each protocol. A summary of all serious or unexpected side effects also must be included in the APR. If there were no adverse events, this must be stated on the APR.

6.6 Human Biological Specimens/Tissue (HBS/tissue): N/A

6.7 Subject Confidentiality Protection

Demographic (age and sex) and clinical data will be entered directly from the medical record into a database. This database will be restricted to members of the research team in the Center for Refractive Surgery.

6.7.1 Certificate of Confidentiality

Not applicable.

6.7.2 HIPAA Authorization

i. Are you intending to collect subject's Protected Health Information (PHI) and any of the following 18 personal identifiers?

☐ No – HIPAA does not apply – go to question #iv

☒ Yes – please check which ones:

☒ 1. Names

☐ 2. Street address, city, county, 5-digit zip code

☒ 3. Months and dates (years are OK) and ages >89 (unless all persons over 89 years are aggregated into a single category)

☒ 4. Telephone numbers

☒ 5. Fax numbers

☒ 6. E-mail addresses

☒ 7. Social security number

☐ 8. Medical record number

☐ 9. Health plan beneficiary number

☐ 10. Account number

☐ 11. Certificate/license number

☐ 12. Vehicle identification number (VIN) and/or license plate number

☐ 13. Device identifiers and serial numbers

☐ 14. URLs (Uniform Resource Locators)

☐ 15. Internet protocol address number

☐ 16. Biometric identifiers, such as finger and voice prints

☐ 17. Full face photographic images or any comparable images

☐ 18. Any other unique identifying number, characteristic, or code such as patient initials

ii. Can you limit your collection of personal identifiers to just dates, city/state/zip, and/or “other unique identifier” (#18 of the above)?

☐ Yes – then your dataset may qualify as a Limited Data Set – please complete a Data Use Agreement and attach to your protocol. Then go to question #iv.

☒ No – Go to question #iii.

iii. Is obtaining patient Authorization “impracticable”?

☐ Yes – Authorization may qualify to be waived by the IRB. Go to Section 6.7.3 HIPAA Authorization Waiver for the application.

☒ No – Research subjects will need to sign a HIPAA Authorization. Complete the HIPAA Authorization and attach to this protocol.

- iv. What precautions will you take to protect the confidentiality of research source documents (Case Report Forms, questionnaires, etc.), the research data file, and the master code (if any)?

A folder will be maintained on each patient. It will include a copy of the consents, patient information sheets, operative report, and any other related correspondence. Patient data obtained during baseline and follow-up examinations will be recorded on worksheets and will be maintained in the patient folder with a unique study ID for each patient based of the randomization table (similar to the flip of a coin), see page 28. No master code will be kept. All study records will be kept in a locked file cabinet by the study coordinator in the Walter Reed Center for Refractive Surgery. The study coordinator (Lamarr Peppers), principal investigator, or a selected designee, will be the only personnel with access to the study files.

- v. When will you destroy the research source documents, data file, and the master code?

The information will be stored at Walter Reed's Center for Refractive Surgery for a maximum of 7 years.

- vi. Will research data including Identifiable Protected Health Information be sent outside of WRAMC?
Yes – Please explain assurances you have received from the outside party that they will appropriately follow confidentiality protections, follow the HIPAA requirements, and abide by the provisions of your Authorization.
X No

Data will be shared with others only as addressed in this protocol, and the HIPPA, and informed consent statements.

6.7.3 HIPAA Authorization Waiver

Not requested.

6.8 Reporting Protocol Deviations

Any protocol deviations during the course of the study will be promptly reported to DCI/IRB and sponsor if applicable, through the medical monitor of the protocol if applicable. Examples of deviations include but are not limited to variances from the treatment schedule for an individual patient, failure to use the most current consent form, and/or incomplete or lost records.

Reporting protocol deviation will be accomplished by submitting a protocol deviation memorandum to the IRB via DCI.

7. REFERENCES

1. Mastropasqua L, Toto L, Zuppari E, et al. Photorefractive keratectomy with aspheric profile of ablation versus conventional photorefractive keratectomy for myopia correction: six-month controlled clinical trial. J Cataract Refract Surg. 2006; 32:109-116.
2. Vongthongsri A, Phusitphoykai N, Naripthapan P. Comparison of wavefront-guided customized ablation vs. conventional ablation in laser in situ keratomileusis. J Refract Surg. 2002 May; 18:S332-335.
3. Mastropasqua L, Nubile M, Ciancaglini M, et al. Prospective randomized comparison of wavefront-guided and conventional photorefractive keratectomy for myopia with the meditec MEL 70 laser. J Refract Surg. 2004; 20:422-31.

4. McDonald MB. Summit-Autonomous and CustomCornea laser in situ keratomileusis outcomes. *J Refract Surg* 2000; 16:S617-618.
5. Buzzonetti L, Petrocelli G, Valente P, et al. Comparison of corneal aberration changes after laser in situ keratomileusis performed with mechanical microkeratome and IntraLase femtosecond laser: 1-year follow-up. *Cornea*. 2008; 27:174-179.
6. Durrie DS, Kezirian GM. Femtosecond laser versus mechanical keratome flaps in wavefront-guided laser in situ keratomileusis: prospective contralateral eye study. *J Cataract Refract Surg*. 2005; 31:120-126.
7. Stonecipher KG, Kezirian GM. Wavefront-optimized versus wavefront-guided LASIK for myopic astigmatism with the ALLEGRETTO WAVE: three-month results of a prospective FDA trial. *J Refract Surg*. 2008; 24:S424-430.
8. Padmanabhan P, Mrochen M, Basuthkar S, et al. Wavefront-guided versus wavefront-optimized laser in situ keratomileusis: contralateral comparative study. *J Cataract Refract Surg*. 2008; 34:389-397.
9. Marcos S. Aberrations and visual performance following standard laser vision correction. *J Refract Surg* 2001;17(5):S596-601.
10. Cano D, Barbero S, Marcos S. Comparison of real and computer-simulated outcomes of LASIK refractive surgery. *J Opt Soc Am A Opt Image Sci Vis* 2004;21(6):926-36.
11. Llorente L, Barbero S, Merayo J, Marcos S. Total and corneal optical aberrations induced by laser in situ keratomileusis for hyperopia. *J Refract Surg* 2004;20(3):203-16.
12. Marcos S, Barbero S, Llorente L, Merayo-Llodes J. Optical response to LASIK surgery for myopia from total and corneal aberration measurements. *Invest Ophthalmol Vis Sci* 2001;42(13):3349-56.
13. Marcos S, Cano D, Barbero S. Increase in corneal asphericity after standard laser in situ keratomileusis for myopia is not inherent to the Munnerlyn algorithm. *J Refract Surg* 2003;19(5):S592-6.
14. Moreno-Barriuso E, Lloves JM, Marcos S, et al. Ocular aberrations before and after myopic corneal refractive surgery: LASIK-induced changes measured with laser ray tracing. *Invest Ophthalmol Vis Sci* 2001;42(6):1396-403.
15. Chalita MR, Chavala S, Xu M, Krueger RR. Wavefront analysis in post-LASIK eyes and its correlation with visual symptoms, refraction, and topography. *Ophthalmology* 2004;111(3):447-53.
16. Chalita MR, Krueger RR. Correlation of aberrations with visual acuity and symptoms. *Ophthalmol Clin North Am* 2004;17(2):135-42, v-vi
17. Chalita MR, Xu M, Krueger RR. Correlation of aberrations with visual symptoms using wavefront analysis in eyes after laser in situ keratomileusis. *J Refract Surg* 2003;19(6):S682-6.
18. Applegate RA, Sarver EJ, Khemsara V. Are all aberrations equal? *J Refract Surg* 2002;18(5):S556-62.
19. Applegate RA, Marsack JD, Ramos R, Sarver EJ. Interaction between aberrations to improve or reduce visual performance. *J Cataract Refract Surg* 2003;29(8):1487-95.
20. Applegate RA, Ballentine C, Gross H, et al. Visual acuity as a function of Zernike mode and level of root mean square error. *Optom Vis Sci* 2003;80(2):97-105
21. Ginsburg AP. Contrast sensitivity: determining the visual quality and function of cataract, intraocular lenses and refractive surgery. *Curr Opin Ophthalmol* 2006;17(1):19-26
22. Mastropasqua L, Nubile M, Ciancaglini M, et al. Prospective randomized comparison of wavefront-guided and conventional photorefractive keratectomy for myopia with the meditec MEL 70 laser. *J Refract Surg* 2004;20(5):422-31.
23. Liang J, Grimm B, Goelz S, Bille JF. Objective measurement of wave aberrations of the human eye with the use of a Hartmann-Shack wave-front sensor. *J Opt Soc Am A* 1994;11(7):1949-57.
24. Tuan KM, Liang J. Improved contrast sensitivity and visual acuity after wavefront-guided laser in situ keratomileusis: in-depth statistical analysis. *J Cataract Refract Surg* 2006;32(2):215-20.
25. Kezirian GM, Stonecipher KG. Comparison of the IntraLase femtosecond laser and mechanical keratomes for laser in situ keratomileusis. *J Cataract Refract Surg* 2004;30(4):804-11.

26. Durrie DS, Kezirian GM. Femtosecond laser versus mechanical keratome flaps in wavefront-guided laser in situ keratomileusis: prospective contralateral eye study. *J Cataract Refract Surg* 2005;31(1):120-6.
27. Netto MV, Dupps W, Jr., Wilson SE. Wavefront-guided ablation: evidence for efficacy compared to traditional ablation. *Am J Ophthalmol* 2006;141(2):360-8.
28. van Heel A. Correcting the spherical and chromatic aberrations of the eye. *Journal of the Optical Society of America* 1946;36:237-9.
29. Coleman H. The reduction in image contrast caused by the aberrations in telescopic systems. *Journal of the Optical Society of America* 1947;37:684-6.
30. Overington I, Gullick S. Evaluation of a total system - optics plus operator. *Opt Acta* 1973;20:49-58.
31. Charman WN, Whitefoot H. Astigmatism, accommodation, and visual instrumentation. *Appl Opt* 1978;17:3903-10
32. Burton GJ, Haig ND. Effects of the Seidel aberrations on visual target discrimination. *J Opt Soc Am A* 1984;1(4):373-85.
33. Lyons K, Mouroulis P, Cheng D. Effect of instrumental spherical aberration on visual image quality. *Journal of the Optical Society of America* 1996;13(2):193-205.
34. Vollmerhausen R, Jacobs E, Driggers R. New Metric for predicting target acquisition performance. *Optical Engineer* 2004;43(II):2806-18
35. Thibos LN, Wheeler W, Horner D. Power vectors: an application of Fourier analysis to the description and statistical analysis of refractive error. *Optom Vis Sci* 1997;74(6):367-75.
36. Thibos LN, Hong X, Bradley A, Cheng X. Statistical variation of aberration structure and image quality in a normal population of healthy eyes. *J Opt Soc Am A Opt Image Sci Vis* 2002;19(12):2329-48.
37. Vollmerhausen R, Jacobs E, Hixson J, Friedman M. The Targeting Task Performance (TTP) Metric: A New Model for Predicting Target Acquisition Performance. Technical Report AMSEL-NV-TR-230 Ft. Belvoir: U.S. Army CERDEC, 2005.
38. Vollmerhausen R, Driggers R, Tomkinson M. Improved image quality metric for predicting tactical vehicle identification. In: Holst GC, ed. *Infrared Imaging Systems: Design, Analysis, Modeling, and Testing XI: Proceedings of SPIE*, 2000; v. 4030.
39. O'Kane B, Page G, Wilson D, Bohan D. Cycle criteria for detection of camouflaged targets. *Proceedings of the NATO Panel on Sensors and Sensor Denial by Camouflage, Concealment and Deception*. Brussels, Belgium, 2004
40. Self M, Miller B, Dixon D. Acquisition level definitions and observables for human targets, urban operations, and the The Global War on Terror. US Army AMSRD-CER-NV-TR-235. Ft. Belvoir: U.S. Army Communications and Electronics Command Night Vision and Electronic Sensors Directorate 2005.

8. FACILITIES/ORGANIZATIONS TO BE USED

Ophthalmology Clinic, Walter Reed Army Medical Center, Washington, DC.

All baseline and post-operative clinical measurements, including refractions, slit lamp examination, glare testing, forward light scatter measurements, and contrast sensitivity will be determined by eye clinic personnel at WRAMC laser.

Night Vision Lab, Night Vision & Electronic Sensors Directorate, Ft. Belvoir, VA.

Night Vision Task Performance and firing range performance will be performed by trained staff in the Night Vision Lab.

9. ROLE AND RESPONSIBILITIES OF EACH INVESTIGATOR AND COLLABORATOR

COL Kraig S. Bower, MD will serve as Principal Investigator and ensure that the study is conducted in full compliance with applicable rules and regulations. Will oversee all medical aspects of the evaluation and treatment of subjects, including all surgical procedures. Will ensure that study personnel are appropriately trained and that surgeons have adequate training and skills, along with appropriate oversight, in the performance of surgical procedures. Will oversee protocol development, data collection and analysis, manuscript preparation, and presentation and publication of results. Will ensure that study personnel adhere to protocol techniques and methods. Will manage research budget to ensure fiscal responsibility within the terms of the research grant. Will oversee hiring and firing of laser center personnel and all aspects of the operation of the laser center.

LTC Charles D. Coe, PhD will serve as principal scientist for the study at WRAMC. He will supervise or conduct in-processing medical exam, medical records screening and the pre- and post-operative examinations conducted at WRAMC. He will oversee protocol development, data collection and analysis, manuscript preparation, and presentation and publication of results. Will ensure that study personnel adhere to protocol techniques and methods. He will supervise or perform all data analysis, including wavefront transformations and contrast sensitivity data transformation for NVESD prediction modeling.

LTC Richard A. Stutzman, MD will serve as the Study Physician and Ophthalmologist at WRAMC. He will conduct the in-processing medical exam, medical records screening and the ophthalmological evaluations for all applicants to the study being screened at WRAMC. He will also serve as associate investigator and ensure that the study is conducted in full compliance with applicable rules and regulations. Will oversee protocol development, data collection and analysis, manuscript preparation, and presentation and publication of results. Will ensure that study personnel adhere to protocol techniques and methods.

Jayson Edwards, M.D. will serve as associate investigator and ensure that the study is conducted in full compliance with applicable rules and regulations. Will oversee protocol development, data collection and analysis, manuscript preparation, and presentation and publication of results. Will ensure that study personnel adhere to protocol techniques and methods.

Denise Sediq, M.S. will serve as associate investigator and assist in protocol development, data collection and analysis, manuscript preparation and presentation and publication of results.

Chrystyna Kuzmowych, O.D. will serve as Optometrist for the study at WRAMC. She will assist in the in-processing medical exam, medical records screening and the pre- and post-operative examinations conducted at WRAMC.

Jennifer Eaddy, O.D. will serve as an Optometrist for the study at WRAMC. She will assist in the in-processing medical exam, medical records screening and the pre- and post-operative examinations conducted at WRAMC.

Lamarr Peppers will serve as Study Coordinator for the study at WRAMC. He will conduct medical records screening, scheduling and obtain consents for all applicants to the study being screened or enrolled in the study at WRAMC.

Barbara O’Kane, Ph.D. will oversee all testing procedures in the Night Vision Laboratory. Will assist with protocol development and ensure that night vision test procedures are developed and conducted in standardized fashion by trained personnel in a safe environment. Will coordinate budget to cover cost of equipment and personnel involved in testing. Will assist in analysis of night vision detection and

identification data as well as firing range data. Will assist with manuscript preparation for publication in peer-reviewed literature and presentation at local, national and international meetings.

Brian Miller will oversee all testing procedures in the Night Vision Laboratory. Will assist with protocol development and ensure that night vision test procedures are developed and conducted in standardized fashion by trained personnel in a safe environment. Will coordinate budget to cover cost of equipment and personnel involved in testing. Will assist in analysis of night vision detection and identification data as well as firing range data. Will assist with manuscript preparation for publication in peer-reviewed literature and presentation at local, national and international meetings.

10. TIME REQUIRED TO COMPLETE THE RESEARCH (INCLUDING DATA ANALYSIS) –

Anticipated start date – 1 Oct 2008

Expected completion date – 3 Oct 2010

11. BUDGET

Will any outside organization provide funding or other resources? Yes (XX) No ()

The PI has applied for a Peer Reviewed Medical Research Program (PRMRP) grant through the Department of Defense Congressionally Directed Medical Research Programs (CDMRP). [Topic area: Eye and Vision Research]. Award notification will be made after December 2008. No funding is requested from DCI for this protocol. If the award is granted the Henry M. Jackson Foundation will receive the award and administer the funding for this study. A budget page will be submitted if approval for the funding is granted.

12. ENVIRONMENTAL IMPACT STATEMENT (*May be revised IAW future DCI SOP)**

Does any part of this protocol generate any of the following regulated waste?

- | | |
|------------------------------------|--------------------------|
| a. Hazardous chemical waste | Yes () No (XX) |
| b. Regulated Medical Waste | Yes () No (XX) |
| c. Radioactive Waste | Yes () No (XX) |

If yes to any, please indicate at what stage and how much? N/A

13. INVESTIGATOR COMPLIANCE STATEMENT (May be revised IAW DCI SOP)

a. I have read and understand the provisions of The Belmont Report, Ethical Principal and Guidelines for the Protection of Human Subjects of Research, April 18, 1979.

b. I have read and will comply with WRAMC DOD Assurance and WRAMC Federal-Wide Assurance for the protections of human subjects from research risks.

c. I have read and will comply with the institutional policies and guidelines as outlined in the Standard Operating Procedures (SOP) of the Department of Clinical Investigation and the Principal Investigator Guide. (See DCI web-site for a copy,
http://www.wramc.amedd.army.mil/departments/dci/NCA_Web/NCA_WebPage.htm)

d. I have read and will comply with the “Potential Conflict of Interest in Clinical Research at WRAMC as outlined in the DCI SOP.

e. I certified that any outside funds and/or other resources (other than requested from DCI) being provided for this study are listed above in this application under Section II- Budget.

14. RESPONSIBILITIES OF THE PRINCIPAL/ASSOCIATE INVESTIGATOR IN HUMAN SUBJECTS RESEARCH (May be revised IAW future DCI SOP)**

The principal investigator is the individual who is primarily responsible for the actual execution of the clinical investigation. He/she is responsible for the conduct of the study, obtaining subjects' consent, providing necessary reports, and maintaining study documents. The Associate Investigator will assist the Principal Investigator for the responsibilities stated below.

As the Principal Investigator or Associate Investigator:

a. I will not enroll a subject into a study until the study has been approved by the appropriate authority and, when appropriate, the subject's primary care physician has granted approval for him/her to enter a study.

b. By signing this protocol, I warrant that any use of Protected Health Information (PHI) for reviews preparatory to research met the following requirements:

- i. The review of PHI was done solely to prepare a research protocol, or for similar purposes preparatory to research;
- ii. No PHI was taken outside the Military Health System; and
- iii. This review of PHI was necessary for research purposes

c. I am responsible for assuring that the prospective volunteer is not participating as a subject in other research that will significantly increase the research risks.

d. I am responsible for assuring the quality of each subject's consent in accordance with current federal regulations. This will include ensuring that any "designee" that obtains consent on my behalf is completely conversant with the protocol and is qualified to perform this responsibility.

e. I will obtain the WRAMC IRB approval for advertisements used to recruit research subjects.

f. I will not accept any outside personal remuneration for implementation of a study.

g. I will take all necessary precautions to ensure that the study does not generate hazardous chemical waste.

h. I will obtain the proper WRAMC clearance prior to all presentations, abstracts, and publications. The following require WRAMC approval:

- i. Reports involving WRAMC subjects and/or patients.
- ii. Reports that cite WRAMC in the title or byline.
- iii. Reports of WRAMC approved clinical investigation or research.
- iv. Reports of research performed at WRAMC.
- v. Reports of research conducted by WRAMC assigned personnel.

i. I must submit to the Department of Clinical Investigation (DCI):

- i. Any source of outside funding.
- ii. An APR, due in the anniversary month of the protocol's initial approval or due in the month as determined by the IRB for continuing review and approval.
- iii. Reports of adverse effects occurring in subjects as a result of study participation or of any protocol deviations and submit these reports to Medical Monitor if there is one for the study.
- iv. An Addendum, prior to any changes made to the study or a change in the funding status.

- v. A Final Report within 30 days following termination of a study.
- vi. Listing of presentations, abstracts, and publications arising from the study for inclusion in the APR.

j. I will maintain a Study File that must be kept for three years following completion of the study if no IND/IDE used (32 CFR 219.115(b)). If IND medication or IDE appliances are used, the file must be kept for 2 years after FDA approval and can then be destroyed; or if no application is filed or approved, until 2 years after the study is discontinued and FDA notified (21CFR 312.62(c)). The records should be kept in the Department/Service where the research took place (AR 40-38). If I am scheduled to PCS or ETS, these records will be given to a new WRAMC PI or the Department/Service Chief.

This file may be inspected at any time by DCI, (**future 2nd tier office), Department of the Defense (DOD), the Food and Drug Administration (FDA), and/or other regulatory agencies responsible for the oversight of research. This file will include:

- i. The approved protocol and applicable addenda.
- ii. The WRAMC Scientific Review Board and IRB minutes (as appropriate) and the DCI memorandum granting approval to begin the study.
- iii. Other applicable committee minutes [e.g., Radioactive Drug Research Committee (RDRC); the Surgeon General's Human Subjects Research Review Board].
- iv. Each Volunteer Agreement Affidavit (i.e., consent form) signed by the subject.
- v. APR or Final Report.
- vi. Reports of adverse effects occurring in subjects as a result of study participation.
- vii. Reports of any significant new findings found during the course of the study.
- viii. All study documents generated from study date, e.g., patient enrollment log research records, data collection sheets, etc.
- ix. Publications/abstracts/Presentations Clearance documents, and reprints from study data
- x. All information pertaining to an investigational drug or device.
- xi. For HIV research studies, approval of the Chief, Infectious Disease Service.

k. I will be familiar with all applicable regulations governing research, and will adhere to all of the requirements outlined in the WRAMC's DOD Assurance and Federal-Wide Assurance granted by the Office for Human Research Protections, Department of Health and Human Services.

15. MEDICAL MONITOR RESPONSIBILITIES

(***May be revised IAW future DCI SOP.)

Duties as the Medical Monitor include:

- 1) Monitoring the conduct of the protocol per the approval plan and ensuring protection of human subjects. This may involve periodic review of medical records of enrolled subjects and the research files being maintained by the PI.
- 2) Reviewing and keeping abreast of adverse events and protocol deviations that occur during the research; (all adverse events, including deaths and serious or unexpected side effects, are reported to the Medical Monitor via the PI).
- 3) If there is concern about the welfare of enrolled subjects, the Medical Monitor has the authority to stop a research study in progress, remove individual subject from a study, and take whatever steps necessary to protect the safety and well being of research subjects until the IRB can assess the Medical Monitor's report. Notification of such actions must be forwarded to the DCI within one (1) working day of receipt of knowledge prompting human subject welfare concerns.

take whatever steps necessary to protect the safety and well being of research subjects until the IRB can assess the Medical Monitor's report. Notification of such actions must be forwarded to the DCI within one (1) working day of receipt of knowledge prompting human subject welfare concerns.

- 4) Medical Monitors will be required to co-sign all adverse event reports, protocol deviation memoranda, APR, and addendum.
- 5) The Medical Monitor must keep current the WRAMC required research ethics Human Subjects Training every 3 years.
- 6) If the Medical Monitor is expected to be away for more than 14 days but less than 30, the PI or Medical Monitor must designate an acting Medical Monitor and document such action.
- 7) If a Medical Monitor leaves WRAMC for greater than 30 days then the PI must be informed to designate a new Medical Monitor and report such change to the IRB via a memorandum for a change of Medical Monitor (see template).

16. PRINCIPAL INVESTIGATOR SIGNATURE

With my signature, I acknowledge that I have read and am accountable for the responsibilities under Section 13 and Section 14. I understand that if I fail to comply with any of these responsibilities, all projects for which I am an investigator may be suspended. I also acknowledge the above Application for Clinical Investigation Project; Request for Approval of Clinical Investigation Study Proposal; Environmental Impact Statement; Investigator Compliance Statement; and Responsibilities of the Principal/Associate Investigator in Human Subject Research.



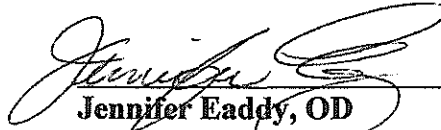
COL Kraig S. Bower, USA MC
Director, Center for Refractive Surgery
Ophthalmology Service
Walter Reed Army Medical Center

17. ASSOCIATE INVESTIGATOR SIGNATURE

With my signature, I acknowledge that I have read the responsibilities under Section 13 and Section 14 and will comply with them.



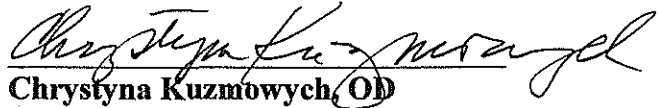
Richard D. Stutzman, MD
LTC USA MC
Ophthalmology Service
Walter Reed Army Medical Center



Jennifer Eaddy, OD
Staff Optometrist
Center for Refractive Surgery
Walter Reed Army Medical Center



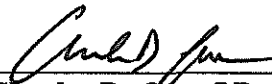
Jayson D. Edwards, MD
Research Associate
Center for Refractive Surgery
Walter Reed Army Medical Center



Chrystyna Kuzmowych, OD
Staff Optometrist
Center for Refractive Surgery
Walter Reed Army Medical Center



Denise A. Sedig, MS
Research Associate
Center for Refractive Surgery
Walter Reed Army Medical Center

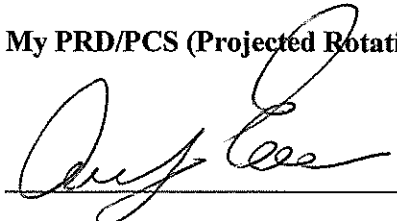


Charles D. Coe, OD, PhD
LTC USA MSC
Director, Refractive Research
Center for Refractive Surgery
Walter Reed Army Medical Center

18. MEDICAL MONITOR

With my signature, I acknowledge that I have read the responsibilities under Section 15 and agreed to serve as Medical Monitor for the above protocol. I understand that the Medical Monitor must be independent of the research study, i.e., not an investigator of the study and cannot be a subordinate in the PI's rating scheme because of a potential for command influence type conflict of interest.

My PRD/PCS (Projected Rotation Date/Permanent Change of Station Date) is None.



(Signature Required)

MEDICAL MONITOR

COL Andrew S. Eiseman, USA MC

Assistant Chief, Ophthalmology Clinic

Program Director

Ophthalmology Service, Department of Surgery

19. DEPARTMENT CHIEF AND SERVICE CHIEF SIGNATURE

I concur with the submission of this proposal to the Clinical Investigation Committee and/or Human Use Committee for review and approval.



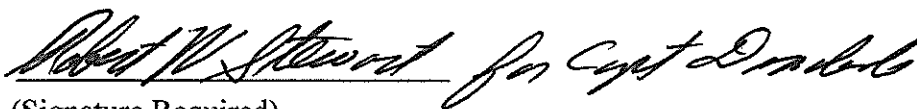
(Signature Required)

SERVICE CHIEF

William R. Rimm, MD

COL USA MC

Chief, Ophthalmology Service



(Signature Required)

DEPARTMENT CHIEF

John W. Denobile, MD, FACS

CAPT, MC, USN

Chief, Integrated Department of Surgery

Walter Reed Army Medical Center and

National Naval Medical Center

20. APPENDICES

As appropriate include all relevant documents in the following sequences:

APPENDIX A – Figures / Graphs

APPENDIX B - Data collection sheets / Case Report Forms / Questionnaires (include the author's permission to use questionnaires/surveys, as applicable)

APPENDIX C – Signed General Impact Statement

APPENDIX D - All Other Impact Statements signed by applicable Departments, such as:

- Nursing Impact Statement
- Pathology Impact Statement if study involves the Pathology Department
- Pharmacy Impact Statement if study uses any drugs, IND or otherwise
- Telemedicine Impact Statement if study uses Telemedicine facilities
- The Military Amputee Center Impact Statement
- Directorate of Information Technology and Management

APPENDIX E – Signed Conflict of Interest Statement

APPENDIX F - Support Letters/Documents

- Letters re: loaned equipment
- Letters of support from Collaborators and/or Consultants
- Cooperative Research and Development Agreement (CRADA)

APPENDIX G - Advertisement Brochure/Flyer – N/A

APPENDIX H - Consent Form(s)

APPENDIX I - HIPAA Authorization Form

APPENDIX J – N/A

If extra-mural study, provide a copy of the sponsor's protocol

If an Investigational New Drug (IND) study, provide the signed original of the FDA Form 1572 (Statement of Investigator) and/or FDA Form 1571 (if PI is the IND Applicant). The FDA Forms are at <http://www.fda.gov/opacom/morechoices/fdaforms/cder.html>.

For more information, please refer to the Principal Investigator Guide at DCI web site or Contact DCI at 202 782-6389.

(Version - WRAMC Human Use Protocol.doc, 16 November 07

Data Forms

Refractive Surgery Preoperative Examination

Patient Name: _____ SSN: _____

Rank: _____ Age: _____ Job: _____ Date: _____

☐ WFO PRK ☐ WFO LASIK ☐ WFG PRK ☐ WFG LASIK SUB PROTOCOL: **Yes / No**

Questionnaire complete (staff initials): _____

Medical Hx/Meds: _____ Allergies: _____

CL Hx: ☐ N/A ☐ DWSCL ☐ EWSCL ☐ RGPCL (see doc)

Notes:

Dominant Eye (check)

☐ Right

☐ Left

Present Rx

(_____)

How old?

_____ — _____ X _____ — _____ X _____

Auto Refraction

_____ — _____ X _____ — _____ X _____

Auto Keratometry

_____ X _____ @ _____ X _____ @ _____

Flat
axis

Flat
axis

Uncorrected VA

20/ _____

20/ _____

Manifest Refraction

_____ — _____ X _____ — _____ X _____

Best Corrected VA

20/ _____

20/ _____

5% Contrast (low light)

20/ _____

20/ _____

25% Contrast (low light)

20/ _____

20/ _____

Super Vision Test

20/ _____

20/ _____

Dilating drops

☐ Mydracyl 1%

☐ Phenylephrine 2.5%

☐ Cyclogel 1%

@ _____

Auto Refraction

_____ — _____ X _____ — _____ X _____

Cycloplegic Refraction

_____ — _____ X _____ — _____ X _____

Pachymetry _____ , _____ , _____

_____ , _____ , _____

Intraocular Pressure _____ mmHg

_____ mmHg @ _____

Tech stamp

Topography ☐ Pentacam
Wavefront (undilated/ dilated)
CSF

☐ Humphrey
☐ COAS
☐ Cambridge

☐ Super Vision Test
☐
☐ Other: _____

Pupil (low light) device: _____ mm

_____ mm

Slit Lamp Exam: Right

Left

☐

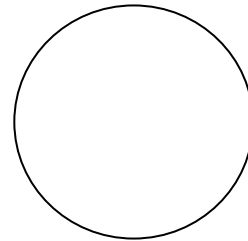
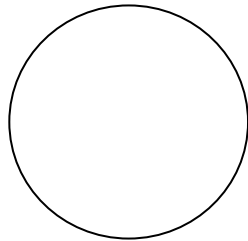
Normal

☐☐

Abnormal

☐

(detailed notes required)



Fundus/Retina (as indicated):

☐

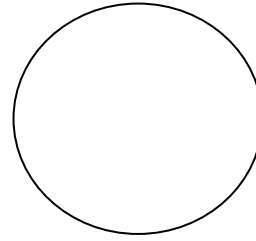
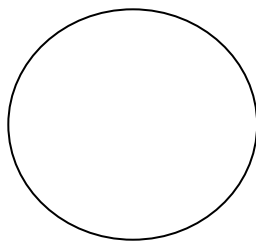
Normal

☐☐

Abnormal

☐

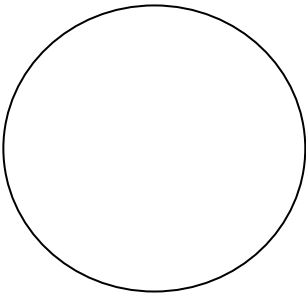
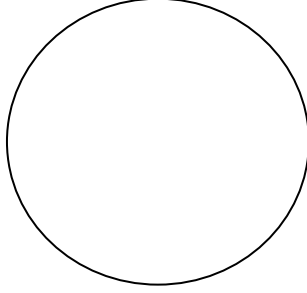
(detailed notes required)



Assessment/Plan:

Investigator _____

Immediate Post-Op Examination

Patient:			Rank:		Last 4 ssn:													
Surgery date:																		
Exam date:			OD		OS													
P/op day 1 2 3 4 5 6			UCVA		BCL													
Med usage (# pills or drops/day):			20/		20/													
Motrin																		
Tylenol																		
Percocet			Slit Lamp Exam: <input type="checkbox"/> Normal/Expected PostOp Findings <input type="checkbox"/> Abnormal/Unexpected PostOp Findings (detailed notes required)  Epi defect: <input type="checkbox"/> none _____ mm x _____ mm		Slit Lamp Exam: <input type="checkbox"/> Normal/Expected PostOp Findings <input type="checkbox"/> Abnormal/Unexpected PostOp Findings (detailed notes required)  Epi defect: <input type="checkbox"/> none _____ mm x _____ mm													
Phenergan																		
Tetracaine																		
Art.Tears																		
Antibiotic																		
Steroid																		
Chief Complaint:																		
(0=none, 1=trace, 2=mild, 3=mod, 4=sev) <table border="1" style="display: inline-table; margin-left: 10px;"> <tr> <th colspan="2">Symptoms</th> </tr> <tr> <th>OD</th> <th>OS</th> </tr> <tr> <td>Pain</td> <td></td> </tr> <tr> <td>Tearing</td> <td></td> </tr> <tr> <td>FB Sensation</td> <td></td> </tr> <tr> <td>Photophobia</td> <td></td> </tr> </table>							Symptoms		OD	OS	Pain		Tearing		FB Sensation		Photophobia	
Symptoms																		
OD	OS																	
Pain																		
Tearing																		
FB Sensation																		
Photophobia																		
Doctors Notes:																		
<input type="checkbox"/> Assessment / Plan (if normal exam): 1. Normal postoperative healing / recovery 2. Compliant w/ meds: <input type="checkbox"/> Yes <input type="checkbox"/> No 3. Continue medications as prescribed 4. Steroid taper: <input type="checkbox"/> N/A <input type="checkbox"/> 8 wks <input type="checkbox"/> 4 mos 5. Follow up in: _____ day(s) or _____ week(s)				<input type="checkbox"/> Assessment / Plan (if other than normal exam): <div style="height: 100px;"></div>														

Provider printed name or stamp

Provider signature

Refractive Surgery Postoperative Examination

Patient Name: _____ SSN: _____

Rank: _____ Age: _____ Job: _____ Date: _____

Surgery Date

1wk 1mo 3mo 6mo 12mo Other

OD: _____

Post-Op

OS: _____

Period:

Unscheduled visit (list reason(s)): _____

Questionnaire complete (staff initials): _____

Eye meds (list): _____

Chief complaint / focused Hx:

Symptoms:

0=none
1=trace
2=mild
3=mod
4=sev

Pain

Tearing

FB sensation

Photophobia

R	L

Right

Left

Auto Refraction

_____ — _____ X _____

_____ — _____ X _____

Auto Keratometry

_____ X _____ @ _____

_____ X _____ @ _____

Uncorrected VA

20/ _____

20/ _____

Manifest Refraction

_____ — _____ X _____

_____ — _____ X _____

Best Corrected VA

20/ _____

20/ _____

5% Contrast (low light)

20/ _____

20/ _____

25% Contrast (low light)

20/ _____

20/ _____

Dilating drops

☐

Mydracil 1%

☐

Phenylephrine 2.5%

☐

Cyclogel 1%

@

Auto Refraction

_____ — _____ X _____

_____ — _____ X _____

Cycloplegic Refraction

_____ — _____ X _____

_____ — _____ X _____

Corneal Sensitivity

_____ cm

_____ cm

Intraocular Pressure

_____ mmHg

_____ mmHg

@

Topography

☐

Pentacam

☐

Humphrey

☐

Super Vision Test

Wavefront (undilated/dilated)

☐

COAS

☐

Other:

CSF

☐

Cambridge

☐

Slit Lamp Exam:

Right

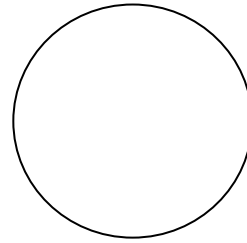
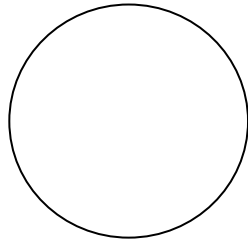
Left

☐

Normal or Expected PostOp Findings

☐☐

Abnormal or Unexpected PostOp Findings
(detailed notes required)

☐☐

Haze (grade 0 to 4+)

☐

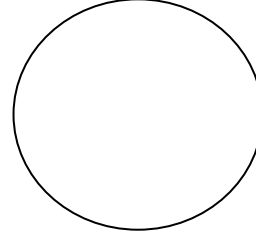
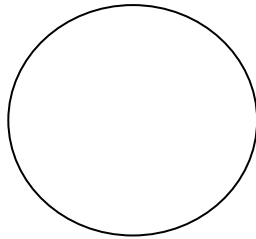
Fundus/Retina (as indicated):

☐

Normal

☐☐

Abnormal
(detailed notes required)

☐

Notes/Plan:

- Normal postoperative recovery and exam
- Patient compliant with medications prescribed

YES

☐
☐

NO (if NO, see notes below)

☐
☐

- Is there an Adverse Event to report at this visit?

☐☐

(if YES, notify PI/Medical Monitor)

Next follow-up exam:

days
 weeks
 months

from now
 post-op

Investigator

Appendix B

Questionnaire Pre-Op

For Night Vision Performance Study

Psychosocial and Visual Characteristics

As part of the military's ongoing studies of refractive surgeries, we are interested in finding out about your current vision. We are interested in **your** opinions and experiences. There are no right or wrong answers. All of the information you provide is confidential and will be published **only** in summary statistical form. You will not be identified in any way.

The information you give us will not affect your eligibility for surgery, your health care, or your vision care in any way. In order to get accurate information about refractive surgeries and how they affect people's vision, we need information from **all** patients.

PLEASE READ EACH QUESTION AND SELECT THE ANSWER THAT BEST REPRESENTS YOU.

Name:	Medical Record #:
Date:	Study ID:

1. This question asks about your **current** use of corrective lenses. In answering these questions please think about your typical use of glasses and/or contact lenses during the **last 30 days**. While you are **AWAKE**, do you predominantly wear glasses or contact lenses in **either** eye to improve your eyesight? Please indicate whether you predominantly wear **contact lenses, glasses** or **neither**.

PREDOMINANTLY WEAR GLASSES.....1

PREDOMINANTLY WEAR CONTACT LENSES.....2

WEAR NEITHER GLASSES NOR CONTACT LENSES.....3

This set of questions asks you to describe your vision as you go about your daily activities , both when you are at work and when you are not at work.

2. In general, is your vision causing you difficulty as you go about your **daily activities**.

No Difficulty

Extreme Difficulty

1. 2. 3. 4. 5. 6. 7. 8. 9. 10

3. Do you have problems with **dry eyes**?

None of the Time

All of the Time

1. 2. 3. 4. 5. 6. 7. 8. 9. 10

4. How many times a day do you use **artificial tears**?

None 1

One time daily 2

Two times daily 3

Three times daily 4

Four times or more daily . . . 5

5. Do you have problems with your **vision fluctuating** over the day?

None of the Time

All of the Time

1. 2. 3. 4. 5. 6. 7. 8. 9. 10

6. How much difficulty do you have because of **double vision or ghost images**?

No Difficulty

Extreme Difficulty

1. 2. 3. 4. 5. 6. 7. 8. 9. 10

A. *If* you experience **double vision or ghost images**, is it in your:

Right eye only 1

Left eye only 2

Both eyes 3

Neither eye 4

GLARE

7. People have different experiences with their vision. Some people have problems with **glare or light sensitivity**. Please indicate whether you now---that is within the **last two weeks**---have problems with **glare or light sensitivity** in any of the following situations.

On a scale of 1 to 10 where **1** stands for “**no glare**” and **10** stands for “**disabling glare**”, how much trouble do you have with **glare**:

	No Glare	Disabling Glare
A. At night?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	
B. During work?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	
C. From oncoming car headlights at night?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	
D. When watching television or using a computer monitor?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	

E. When reading a brightly illuminated road sign at night? 1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10

HALO

8. People have different experiences with their vision. Some people have problems with **halos, rings** or **starbursts** around objects or lights. Please indicate whether you now---that is within the **last two weeks**---have problems with **halos, rings** or **starbursts** in any of the following situations.

On a scale of 1 to 10 where **1** stands for “**no halos**” and **10** stands for “**disabling halos**”, how much trouble do you have with **halos**:

	<i>No</i> Halos	<i>Disabling</i> Halos
A. At night?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	
B. During work?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	
C. From oncoming car headlights at night?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	
D. When watching television or using a computer monitor?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	
E. When reading a brightly illuminated road sign at night?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	

Thank you for your help in completing this questionnaire.

Please return your completed questionnaire to the clinic staff.

Questionnaire Post Op

For Night Vision Performance Study

Psychosocial and Visual Characteristics

As part of the military's ongoing studies of refractive surgeries, we are interested in finding out about your current vision. We are interested in **your** opinions and experiences. There are no right or wrong answers. All of the information you provide is confidential and will be published **only** in summary statistical form. You will not be identified in any way.

The information you give us will not affect your eligibility for surgery, your health care, or your vision care in any way. In order to get accurate information about refractive surgeries and how they affect people's vision, we need information from **all** patients.

PLEASE READ EACH QUESTION AND SELECT THE ANSWER THAT BEST REPRESENTS YOU

Name:		Medical Record #:
Date:	Visit:	Study ID:

1. This question asks about your **current** use of corrective lenses. In answering these questions please think about your typical use of glasses and/or contact lenses during the **last 30 days**. While you are **AWAKE**, do you predominantly wear glasses or contact lenses in **either** eye to improve your eyesight? Please indicate whether you predominantly wear **contact lenses, glasses or neither**.

PREDOMINANTLY WEAR GLASSES.....1

PREDOMINANTLY WEAR CONTACT LENSES.....2

WEAR NEITHER GLASSES NOR CONTACT LENSES.....3

This set of questions asks you to describe your vision as you go about your daily activities , both when you are at work and when you are not at work.

2. In general, is your vision causing you difficulty as you go about your **daily activities**.

No Difficulty

Extreme Difficulty

1. 2. 3. 4. 5. 6. 7. 8. 9. 10

3. Do you have problems with **dry eyes**?

None of the Time

All of the Time

1. 2. 3. 4. 5. 6. 7. 8. 9. 10

4. How many times a day do you use **artificial tears**?

None 1
One time daily 2
Two times daily 3
Three times daily 4
Four times or more daily . . . 5

5. Do you have problems with your **vision fluctuating** over the day?

None of the Time All of the Time
1 2 3 4 5 6 7 8 9 10

6. How much difficulty do you have because of **double vision or ghost images**?

No Difficulty Extreme Difficulty
1 2 3 4 5 6 7 8 9 10

A. *If* you experience **double vision or ghost images**, is it in your:

Right eye only 1
Left eye only 2
Both eyes 3
Neither eye 4

GLARE

7. People have different experiences with their vision. Some people have problems with **glare** or **light sensitivity**. Please indicate whether you now---that is within the **last two weeks**---have problems with **glare** or **light sensitivity** in any of the following situations.

On a scale of 1 to 10 where **1** stands for “**no glare**” and **10** stands for “**disabling glare**”, how much trouble do you have with **glare**:

	<i>No</i> Glare	<i>Disabling</i> Glare
A. At night?	1 . . 2 . . 3 . . 4 . . 5 . . 6 . . 7 . . 8 . . 9 . . 10	
B. During work?	1 . . 2 . . 3 . . 4 . . 5 . . 6 . . 7 . . 8 . . 9 . . 10	
C. From oncoming car headlights at night?	1 . . 2 . . 3 . . 4 . . 5 . . 6 . . 7 . . 8 . . 9 . . 10	
D. When watching television or using a computer monitor?	1 . . 2 . . 3 . . 4 . . 5 . . 6 . . 7 . . 8 . . 9 . . 10	
E. When reading a brightly illuminated road sign at night?	1 . . 2 . . 3 . . 4 . . 5 . . 6 . . 7 . . 8 . . 9 . . 10	

HALO

8. People have different experiences with their vision. Some people have problems with **halos**, **rings** or **starbursts** around objects or lights. Please indicate whether you now---that is within the **last two weeks**---have problems with **halos**, **rings** or **starbursts** in any of the following situations.

On a scale of 1 to 10 where **1** stands for “**no halos**” and **10** stands for “**disabling halos**”, how much trouble do you have with **halos**:

	<i>No</i> Halos	<i>Disabling</i> Halos
A. At night?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	
B. During work?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	
C. From oncoming car headlights at night?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	
D. When watching television or using a computer monitor?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	
E. When reading a brightly illuminated road sign at night?	1 . . . 2 . . . 3 . . . 4 . . . 5 . . . 6 . . . 7 . . . 8 . . . 9 . . . 10	

As people recover from surgery, they sometimes find out that things do not turn out exactly as they expected. As you read the next set of questions think about your experiences **since you had surgery**.

9. In comparison to what you expected before you had surgery, has your **overall vision** turned out to be:

Much Better
than expected

Much Worse
than expected

1 2 3 4 5 6 7 8 9 10

10. Thinking about your **vision during the last two weeks**, if you had it to do over, would **have the surgery today**?

Definitely would
have surgery

Definitely would not
have surgery

1 2 3 4 5 6 7 8 9 10

Randomization Tables

Subjects undergoing testing at Ft. Belvoir

1. PRK, WFG, Firing range_____
2. PRK, WFG, NV performance_____
3. PRK, WFO, Firing range_____
4. LASIK, WFG, Firing range_____
5. LASIK, WFO, NV performance_____
6. PRK, WFO, Firing range_____
7. PRK, WFG, NV performance_____
8. LASIK, WFO, NV performance_____
9. LASIK, WFG, NV performance_____
10. PRK, WFO, NV performance_____
11. LASIK, WFG, NV performance_____
12. PRK, WFG, Firing range_____
13. LASIK, WFO, NV performance_____
14. LASIK, WFG, NV performance_____
15. LASIK, WFO, Firing range_____
16. PRK, WFO, Firing range_____
17. PRK, WFG, NV performance_____
18. PRK, WFO, NV performance_____
19. LASIK, WFG, NV performance_____
20. LASIK, WFG, NV performance_____
21. PRK, WFG, NV performance_____
22. LASIK, WFG, Firing range_____
23. LASIK, WFO, NV performance_____
24. LASIK, WFO, Firing range_____
25. PRK, WFO, Firing range_____
26. LASIK, WFO, NV performance_____
27. LASIK, WFO, Firing range_____
28. PRK, WFG, Firing range_____
29. LASIK, WFG, Firing range_____
30. LASIK, WFO, NV performance_____
31. PRK, WFO, Firing range_____
32. LASIK, WFG, Firing range_____
33. LASIK, WFG, Firing range_____
34. LASIK, WFG, NV performance_____
35. PRK, WFG, NV performance_____
36. PRK, WFO, NV performance_____
37. PRK, WFG, Firing range_____
38. LASIK, WFG, Firing range_____
39. PRK, WFG, Firing range_____
40. LASIK, WFG, Firing range_____
41. PRK, WFG, NV performance_____

42. PRK, WFO, NV performance _____
43. PRK, WFO, Firing range _____
44. PRK, WFG, Firing range _____
45. LASIK, WFG, NV performance _____
46. PRK, WFO, NV performance _____
47. PRK, WFO, NV performance _____
48. LASIK, WFG, NV performance _____
49. PRK, WFG, Firing range _____
50. LASIK, WFO, Firing range _____
51. LASIK, WFG, Firing range _____
52. LASIK, WFO, NV performance _____
53. LASIK, WFO, NV performance _____
54. PRK, WFO, NV performance _____
55. PRK, WFG, NV performance _____
56. LASIK, WFG, Firing range _____
57. PRK, WFG, NV performance _____
58. LASIK, WFG, Firing range _____
59. PRK, WFO, Firing range _____
60. LASIK, WFG, Firing range _____
61. LASIK, WFO, Firing range _____
62. PRK, WFG, Firing range _____
63. PRK, WFO, Firing range _____
64. LASIK, WFG, Firing range _____
65. LASIK, WFG, NV performance _____
66. PRK, WFO, NV performance _____
67. LASIK, WFO, NV performance _____
68. LASIK, WFO, Firing range _____
69. PRK, WFG, Firing range _____
70. PRK, WFG, Firing range _____
71. PRK, WFO, NV performance _____
72. LASIK, WFO, Firing range _____
73. LASIK, WFO, NV performance _____
74. PRK, WFO, Firing range _____
75. LASIK, WFO, Firing range _____
76. PRK, WFG, Firing range _____
77. LASIK, WFO, NV performance _____
78. PRK, WFO, Firing range _____
79. PRK, WFO, NV performance _____
80. LASIK, WFO, NV performance _____
81. LASIK, WFO, Firing range _____
82. PRK, WFO, Firing range _____
83. LASIK, WFO, NV performance _____
84. LASIK, WFG, NV performance _____
85. LASIK, WFG, NV performance _____
86. LASIK, WFO, Firing range _____
87. LASIK, WFG, Firing range _____
88. PRK, WFG, NV performance _____

89. LASIK, WFG, NV performance _____
90. PRK, WFO, NV performance _____
91. LASIK, WFO, Firing range _____
92. LASIK, WFO, Firing range _____
93. PRK, WFO, NV performance _____
94. PRK, WFG, Firing range _____
95. LASIK, WFG, NV performance _____
96. PRK, WFG, NV performance _____
97. PRK, WFO, NV performance _____
98. PRK, WFG, Firing range _____
99. PRK, WFO, Firing range _____
100. PRK, WFO, Firing range _____
101. PRK, WFO, NV performance _____
102. LASIK, WFG, Firing range _____
103. PRK, WFG, Firing range _____
104. PRK, WFG, NV performance _____
105. LASIK, WFG, NV performance _____
106. PRK, WFG, NV performance _____
107. LASIK, WFO, NV performance _____
108. LASIK, WFO, Firing range _____
109. LASIK, WFO, Firing range _____
110. PRK, WFG, NV performance _____
111. PRK, WFG, NV performance _____
112. PRK, WFO, Firing range _____

112 subjects randomized into 1 block
To reproduce this plan, use the seed 12377
Randomization plan created on Wednesday, June 04, 2008 2:36 PM

Subjects not undergoing testing at Ft. Belvoir

1. PRK, WFO
2. LASIK, WFG
3. PRK, WFO
4. LASIK, WFO
5. PRK, WFG
6. PRK, WFO
7. PRK, WFO
8. LASIK, WFO
9. PRK, WFG
10. PRK, WFO
11. PRK, WFO
12. LASIK, WFO
13. LASIK, WFO
14. LASIK, WFO
15. LASIK, WFO
16. PRK, WFO
17. LASIK, WFG
18. PRK, WFG
19. PRK, WFO
20. LASIK, WFO
21. PRK, WFG
22. LASIK, WFO
23. LASIK, WFO
24. PRK, WFO
25. PRK, WFG
26. LASIK, WFG
27. PRK, WFO
28. LASIK, WFG
29. PRK, WFO
30. PRK, WFG
31. PRK, WFG
32. LASIK, WFO
33. PRK, WFO
34. LASIK, WFO
35. LASIK, WFG
36. LASIK, WFG
37. LASIK, WFO
38. PRK, WFG
39. PRK, WFG
40. PRK, WFO
41. LASIK, WFG
42. PRK, WFG
43. LASIK, WFO
44. LASIK, WFO
45. LASIK, WFO

46. PRK, WFG
47. PRK, WFG
48. LASIK, WFG
49. PRK, WFG
50. PRK, WFG
51. PRK, WFG
52. PRK, WFO
53. LASIK, WFO
54. PRK, WFG
55. LASIK, WFG
56. LASIK, WFG
57. LASIK, WFG
58. PRK, WFG
59. PRK, WFG
60. PRK, WFO
61. LASIK, WFG
62. PRK, WFO
63. PRK, WFO
64. LASIK, WFO
65. LASIK, WFG
66. PRK, WFO
67. LASIK, WFG
68. PRK, WFO
69. PRK, WFG
70. PRK, WFG
71. LASIK, WFG
72. LASIK, WFO
73. PRK, WFO
74. PRK, WFO
75. PRK, WFG
76. PRK, WFO
77. LASIK, WFO
78. PRK, WFG
79. PRK, WFG
80. LASIK, WFG
81. LASIK, WFO
82. LASIK, WFO
83. PRK, WFG
84. PRK, WFG
85. PRK, WFG
86. LASIK, WFG
87. LASIK, WFO
88. LASIK, WFG
89. LASIK, WFO
90. LASIK, WFG
91. PRK, WFG
92. LASIK, WFG

93.	PRK,	WFO	
94.	LASIK,	WFO	
95.	LASIK,	WFG	
96.	PRK,	WFO	
97.	LASIK,	WFG	
98.	PRK,	WFO	
99.	LASIK,	WFO	
100.	LASIK,	WFO	
101.	LASIK,	WFG	
102.	LASIK,	WFG	
103.	LASIK,	WFO	
104.	LASIK,	WFG	
105.	PRK,	WFO	
106.	PRK,	WFG	
107.	PRK,	WFO	
108.	LASIK,	WFO	
109.	LASIK,	WFG	
110.	LASIK,	WFG	
111.	LASIK,	WFG	
112.	PRK,	WFO	

112 subjects randomized into 1 block
To reproduce this plan, use the seed 14477
Randomization plan created on Wednesday, June 04, 2008 2:46 PM

**Subjects that have CCT <500 microns selected to PRK
subgroup**

1.	PRK	WFO	
2.	PRK	WFG	
3.	PRK	WFG	
4.	PRK	WFG	
5.	PRK	WFG	
6.	PRK	WFG	
7.	PRK	WFO	
8.	PRK	WFG	
9.	PRK	WFO	
10.	PRK	WFO	
11.	PRK	WFG	
12.	PRK	WFO	
13.	PRK	WFG	
14.	PRK	WFO	
15.	PRK	WFO	
16.	PRK	WFO	
17.	PRK	WFO	
18.	PRK	WFO	
19.	PRK	WFG	
20.	PRK	WFO	
21.	PRK	WFO	
22.	PRK	WFO	
23.	PRK	WFO	
24.	PRK	WFO	
25.	PRK	WFG	
26.	PRK	WFG	
27.	PRK	WFG	
28.	PRK	WFG	
29.	PRK	WFO	
30.	PRK	WFG	
31.	PRK	WFG	
32.	PRK	WFO	
33.	PRK	WFO	
34.	PRK	WFG	
35.	PRK	WFO	
36.	PRK	WFG	
37.	PRK	WFO	
38.	PRK	WFG	
39.	PRK	WFG	
40.	PRK	WFG	
41.	PRK	WFO	
42.	PRK	WFO	
43.	PRK	WFG	

44. PRK WFO _____
45. PRK WFO _____
46. PRK WFG _____
47. PRK WFO _____
48. PRK WFO _____
49. PRK WFO _____
50. PRK WFO _____
51. PRK WFO _____
52. PRK WFG _____
53. PRK WFG _____
54. PRK WFO _____
55. PRK WFG _____
56. PRK WFO _____
57. PRK WFO _____
58. PRK WFG _____
59. PRK WFG _____
60. PRK WFG _____
61. PRK WFG _____
62. PRK WFG _____
63. PRK WFO _____
64. PRK WFO _____
65. PRK WFG _____
66. PRK WFG _____
67. PRK WFG _____
68. PRK WFG _____
69. PRK WFO _____
70. PRK WFG _____
71. PRK WFG _____
72. PRK WFO _____
73. PRK WFO _____
74. PRK WFO _____
75. PRK WFO _____
76. PRK WFG _____
77. PRK WFG _____
78. PRK WFO _____
79. PRK WFG _____
80. PRK WFG _____
81. PRK WFO _____
82. PRK WFG _____
83. PRK WFO _____
84. PRK WFG _____
85. PRK WFO _____
86. PRK WFG _____
87. PRK WFO _____
88. PRK WFO _____
89. PRK WFG _____
90. PRK WFG _____

91.	PRK	WFO	
92.	PRK	WFG	
93.	PRK	WFG	
94.	PRK	WFO	
95.	PRK	WFO	
96.	PRK	WFO	
97.	PRK	WFG	
98.	PRK	WFO	
99.	PRK	WFG	
100.	PRK	WFO	
101.	PRK	WFO	
102.	PRK	WFG	
103.	PRK	WFO	
104.	PRK	WFG	
105.	PRK	WFG	
106.	PRK	WFG	
107.	PRK	WFO	
108.	PRK	WFG	
109.	PRK	WFO	
110.	PRK	WFO	
111.	PRK	WFG	
112.	PRK	WFG	

112 subjects randomized into 1 block
To reproduce this plan, use the seed 16607
Randomization plan created on Tuesday, June 10, 2008 2:59:46 PM

LASIK and PRK 03 November 2008

**WALTER REED ARMY MEDICAL CENTER
WASHINGTON, D.C**

This Clinical Trial consent form is valid only if it contains the IRB stamped date

**Consent for Voluntary Participation in a Clinical Trial (a type of research study) Entitled:
“Optical Quality, Threshold Target Identification, and Military Target Task Performance
After Advanced Keratorefractive Surgery”.**

**Principal Investigator: COL Kraig S. Bower, MC, Ophthalmology Service, Department of
Surgery, phone (202) 782-0202**

Study Site: __ NNMC, __ MGMC, X WRAMC, __ USUHS

1. INTRODUCTION OF THE STUDY

You are being asked to be in this research study because you are active duty U.S. Army Soldier and wear either glasses or contact lenses for nearsightedness or astigmatism (unequal curvature of the eyeball). Your participation is voluntary. Refusal will not result in any penalty or loss of benefits to which you are otherwise entitled, nor will refusal have any affect on your military career status.

2. PURPOSE OF THE STUDY

The purpose of this research project is to evaluate the outcomes of visual performance in nighttime military settings before and after receiving wavefront guided or wavefront optimized laser assisted in situ keratomileusis (LASIK) or photorefractive keratectomy (PRK) surgery. Although daytime vision is often excellent following refractive surgery, there have been reports of night vision changes resulting from PRK and LASIK. The information gained will help investigators determine the overall safety and usefulness of the surgery for Army personnel.

Other studies have shown LASIK and PRK to be safe and effective in the treatment of nearsightedness, farsightedness and astigmatism in civilians and in U.S. Army personnel. In nearsightedness, farsightedness or astigmatism, the clear front surface of your eye, the “cornea”, does not have the proper focusing power. To correct this deficiency you must wear lenses in front of the cornea, either glasses or contacts, in order to see clearly.

Both LASIK and PRK use a machine called an excimer laser to reshape your cornea to try and give it the proper focusing power. In the LASIK procedure a “flap” is made in the cornea using another laser, called a femtosecond laser. The flap is lifted and the excimer laser is used to reshape the cornea underneath. The flap is then replaced and allowed to heal. In the PRK procedure no flap is made. Instead, the outer layer of cells on the clear part of your eye, the corneal epithelium, is removed exposing the layer to be treated by the laser. Use of both lasers to

Approved by the WRAMC HUC/IRB on 03 November 2008 (Per CIRO) for WU # 08-6967.
This form expires on 12 August 2009 Initials MG.



make the flap and reshape the cornea is approved by the Food and Drug Administration (FDA) and the procedure is not considered investigational (experimental).

Both LASIK and PRK surgeries can be either wavefront guided or wavefront optimized. The wavefront guided procedure customizes the laser treatments based on the individual characteristics of the eye being corrected. The wavefront optimized procedure uses laser treatment software that has been designed with certain corrections pre-programmed, although a true and customized wavefront plan is not employed.

3. PROCEDURES TO BE FOLLOWED

If you agree to be in this study you will be randomly assigned (similar to the flip of a coin) to one of four groups. Each group will receive one type of refractive surgery. The types of surgery will be wavefront guided PRK, wavefront guided LASIK, wavefront optimized PRK and wavefront optimized LASIK. Your chances of being assigned to each group are equal. All treatments will take place at the Center of Refractive Surgery, Walter Reed Army Medical Center.

Demographic data, such as age and gender, will be collected during your screening exam in order to provide a correlation with clinical data. You will undergo eye testing before and at 1, 3, 6 and 12 months after the surgical procedure at Walter Reed Army Medical Center as part of the standard of care (SOC). This will involve measuring vision, refraction (the need for glasses), eye pressure, corneal (the clear transparent outer layer of the eye) curvature, corneal clarity, corneal thickness, and contrast sensitivity (testing your vision under different dark to light contrast conditions). On several examinations these tests will be repeated after your eyes have been dilated with eye drops.

As part of this study, you will be asked to undergo some additional eye testing for research purposes at the eye examination before surgery and at the examinations done 1, 3, 6, and 12 months after surgery. Contrast sensitivity will be measured using a Visual Stimulus Generator, which displays a visual stimulus on a computer monitor and measures time to recognition. A topographic (surface) map of your eye will be obtained using a Wavefront Analyzer. In addition, your vision will be measured using the SuperVision test, which utilizes a chart similar to that used to measure standard visual acuity, though with smaller and more precise lettering. You will also be asked to complete a questionnaire before surgery and 1, 3, 6 and 12 months after surgery to determine your satisfaction with the conventional PRK procedure. It will take you approximately 15 minutes to complete the questionnaire each time it is given. Each clinic appointment will last from one to two hours.

If you are a woman capable of having children, you will be asked to have a urine pregnancy test before the surgical procedure. If this test is positive, you will not be able to continue in this study. All health and personal information collected during the study will be protected. Confidentiality will be maintained by assigning a study ID to the collected information and will not be associated with your name. No information collected will leave Walter Reed Army Medical Center.



Some patients (but not all) will also be randomly selected to undergo additional testing at the Night Vision Laboratories at Ft. Belvoir, Virginia 3 times (before surgery, 6 weeks and 6 months after surgery). If you are selected to undergo testing at Ft. Belvoir you will need to arrange your own transportation. The purposes of these tests are to evaluate the effect of the types of surgeries on night vision in a military environment. Testing will be during normal business hours in a facility that simulates nighttime conditions. Those receiving additional testing will be tested for marksmanship with an M16-A2 rifle on a modified range under low light or nighttime conditions, or be evaluated for ability to discriminate thermal night vision targets on a computer monitor. If you are selected for the night vision firing range, you will be trained in the use of night vision goggles (takes approximately 1 hour). If you are selected for night vision sensor testing you will be provided a CD or download link for training software that will familiarize you with the types of targets seen in testing (takes approximately 8 hours).

4. AMOUNT OF TIME FOR YOU TO COMPLETE THIS STUDY

You will be part of this study for a total of 12 months. During this time, you will be asked to visit the clinic up to 10 times. During the first week after surgery, you will be seen the day after surgery, 3 or 4 days after surgery, and one week after surgery. Each visit will last about 15 to 30 minutes. Additional follow-up evaluations will be at 1 month, 3 months, 6 months and 12 months following your surgery. These visits will last up to 1 to 2 hours each. Over the entire twelve months, this will require as much as 10 hours of examination time after the surgery (postoperatively). The standard amount of time for patients not involved in research is eight hours. Research candidates can expect an additional two hours of testing.

If you are selected for additional testing at Ft. Belvoir you will be asked to visit the Night Vision Laboratories 3 times. If you are participating in the night firing range, you will receive training in the use of night vision goggles, which will take approximately 1 hour. Each testing period at the firing range will last up to two hours. If you are participating in the night vision sensor testing, you will be provided training software to complete on your own. This will take approximately 8 hours. Prior to testing at Ft. Belvoir you will undergo refresher training that will last 4 hours. The testing period will last up to 3 hours.

5. NUMBER OF PEOPLE THAT WILL TAKE PART IN THIS STUDY

There will be up to 336 people in total taking part in this study. Up to 112 peoples with corneas less than 500 microns will receive the LASIK and PRK treatment in this portion of the study.

6. POSSIBLE RISKS OR DISCOMFORTS FROM BEING IN THIS STUDY

There are no significant risks that may develop as a result of participation in this study, other than those associated with the procedure itself. None of the testing procedures pose any risk beyond a normal eye examination.

The following are possible risks or discomforts that may develop as a result of undergoing PRK surgery:



- a. Eye discomfort or pain immediately after the procedure. Mild to severe discomfort in the treated eye for several days is common. Eye drops, bandage contact lenses, and oral analgesics are routinely used in the post-operative period to manage pain. In addition, eye patches or other measures may be required during this convalescent period.
- b. Decrease in best-corrected visual acuity (vision with eyeglasses or contact lenses). This complication may occur after up to 7% of treatments. This may improve with treatment. Vision may be treated with glasses post-operatively. Alternatively, contact lenses may be required to improve best-corrected visual acuity. The worst-case would be an inability to correct the visual acuity.
- c. Improper correction. Under-correction (nearsightedness) or over-correction (farsightedness) may occur requiring the use of corrective lenses. There is approximately a 4% chance that you will not achieve 20/40 vision without glasses or contact lenses. You may need to wear glasses or contact lenses after the procedure to attain best vision. Retreatment with another laser procedure may be an option.
- c. Dry eye. Grittiness, scratchiness, foreign body sensation, and fluctuating vision, and sensitivity to dust and smoke are very common in the first 1 to 3 months following surgery. These gradually resolve in the large majority of patients. Up to 5% of patients may have more severe dry eye symptoms that last for a longer period of time. This may require frequent use of lubricant eye drops or other medications to treat the symptoms.
- d. Induced astigmatism. Distortion of vision may require corrective lenses (up to 3%).
- e. Glare and halo from bright lights or halos around lights, especially at night. The glare may be severe enough to cause difficulty driving at night. This usually occurs immediately after the procedure and resolves spontaneously, but may be permanent in approximately 5% of people.
- f. Decrease in contrast sensitivity. This typically occurs immediately after the procedure and usually resolves spontaneously, but may be permanent (up to 3%).
- g. Double vision experienced in one eye. This may occur immediately after the procedure and usually resolves spontaneously as the eye heals. Treatment may be necessary, including corrective lenses or retreatment.
- h. Corneal scarring. Following treatment, your cornea may heal with a scar dense enough to affect the vision (less than 2%). The scar may respond to treatment with medications, but may be permanent and require further surgery, including corneal transplant.
- i. Elevated intraocular pressure. High pressure in the eye may occur while taking eye drops after the procedure (up to 10%). This High pressure usually responds to treatment with topical glaucoma medications.



- j. Recurrent erosions. The corneal epithelium may break down resulting in a painful abrasion. This is treated with topical lubrication and antibiotic medications and may require a therapeutic contact lens (up to 3%).
- k. Microbial keratitis (infection of the cornea) may lead to severe eye damage and loss of vision. Intensive antibiotic therapy is usually required, and surgery may be necessary, including corneal transplant. This complication occurs in less than 0.1% (less than one in one thousand).
- l. Endophthalmitis. A serious and vision threatening infection of the inner tissues of the eye that requires surgery and intensive antibiotics for treatment. Permanent vision loss may result. This complication occurs in less than 0.01% (less than one in ten thousand).
- m. Cataract. Cloudiness of the lens inside the eye, which may reduce vision and require surgery for treatment. (less than 0.1%)

In addition to the above, the following are possible risks or discomforts that may develop as a result of undergoing LASIK surgery:

- n. Flap complications. These occur only with LASIK and may happen at the time of surgery or in the period following the surgery. During surgery, the flap may be cut too thin, incompletely, irregularly, or off-center. These complications may result in irregular healing and loss of vision. In the period following surgery the flap may be dislodged with minor trauma or develop wrinkles (called "striae"), inflammation or debris material under the flap.

Any additional risks that may develop as a result of your participation in this study, other than those associated with the procedure itself, are related to the night firing range. None of the clinical testing procedures pose any risk beyond a normal eye examination. None of the night vision sensor testing has any risks other than those associated with looking at a computer monitor.

The risks associated with use of the M16-A2 rifle are present in this study. Military personnel trained in the use of night vision devices and small arms range activities will supervise all operations of this part of the study. The risks of injury are expected to be similar to those of any military supervised rifle range activity.

While all risks that we know about have been listed above, other risks about which we do not know may occur or be discovered during future studies. If we find that there was a major risk to you that was not known at the time of your participation in the study, and the risk might have some effect on your health, you will be informed.



7. POSSIBLE BENEFITS FROM BEING IN THIS STUDY

You will not benefit from being in this study, but information we learn may help us gain important knowledge about overall safety and usefulness of the wavefront guided surgery for Army personnel.

8. CONFIDENTIALITY/PRIVACY OF YOUR IDENTITY AND YOUR RESEARCH RECORDS

The principal investigator will keep records of your being in this study. These records may be looked at by people from the Walter Reed Department of Clinical Investigation (DCI), the Walter Reed Human Use Committee (HUC), the Army Clinical Investigation Regulatory Office (CIRO), and other government agencies as part of their duties. These duties include making sure that research subjects are protected. Collaborators of the study will not have access to your medical records. Confidentiality of your records will be protected to the extent possible under existing regulations and laws. Complete confidentiality cannot be promised, particularly for military personnel, because information bearing on your health may be required to be reported to appropriate medical or command authorities. Your name will not appear in any published paper or presentation related to this study.

When you enter this study you will be given a study ID number which will not contain any part of your social security number based on a randomization table. This study ID number, not your name or social security number, will be used to label your study data. The randomization table linking your study ID number with your personal identifying information will be kept in a locked file in the Walter Reed Center for Refractive Surgery, and access to it will be restricted to the principal investigator and his designee(s). All clinical and research data will be kept for 7 years.

This research study meets the confidentiality requirements of the Health Insurance Portability and Accountability Act (HIPAA). A HIPAA authorization form for this study will be provided to you separately, and you will be asked to sign that form.

9. CONDITIONS UNDER WHICH YOUR PARTICIPATION IN THIS STUDY MAY BE STOPPED WITHOUT YOUR CONSENT

Your taking part in this study may be stopped without your consent if remaining in the study might be dangerous or harmful to you. Your taking part in this study may also be stopped without your consent if the military mission requires it, or if you become ineligible for medical care at military hospitals. The principal investigator may terminate your participation in this study if you fail to attend the baseline or follow-up examinations or elect not to undergo the laser procedure.

10. ELIGIBILITY AND PAYMENT FOR BEING IN THIS STUDY

You will not be paid for your participation in this research study.



11. COMPENSATION IF INJURED AND LIMITS TO MEDICAL CARE

Should you be injured as a direct result of being in this study, you will be provided medical care for that injury at no cost to you. You will not receive any compensation (payment) for injury. You should also understand that this is not a waiver or release of your legal rights. You should discuss this issue thoroughly with the principal investigator before you enroll in this study.

Medical care is limited to the care normally allowed for Department of Defense health care beneficiaries (patients eligible for care at military hospitals and clinics). Necessary medical care does not include in-home care or nursing home care.

12. COSTS THAT MAY RESULT FROM TAKING PART IN THIS STUDY

There are no more costs to you for taking part in this study. Indirect costs may be incurred through lost duty time. You will have multiple follow up visits as previously outlined, which may take you away from your duty. The procedure is very safe with a low rate of complications.

Most soldiers will be able to return to duty within 24 – 48 hours. If a complication were to develop, the time lost from work would be determined by the complication. Frequently, the complications will be managed on an outpatient basis and no hospitalization expenses are expected.

13. IF YOU DECIDE TO STOP TAKING PART IN THIS STUDY AND INSTRUCTIONS FOR STOPPING EARLY

You have the right to withdraw from this study at any time. If you decide to stop taking part in this study, you should tell the principal investigator as soon as possible. By leaving this study at any time, you in no way risk losing your right to medical care. Some testing or period of observation by the investigators may be recommended for you in order for you to safely stop taking part in this study. Any new significant finding during the course of this study that might affect your willingness to continue participation will be communicated to you.

14. STEPS TAKEN BEFORE AND DURING THIS STUDY TO PROTECT YOU

The surgery will be conducted according to manufacturer's guidelines and in the same way as it would be done if you were not taking part in this study. You will be carefully monitored for complications of the surgery. Any undesired, clinically significant change in the eye or eyes operated on will be evaluated and treated by investigators.

To decrease the likelihood of an incorrect power correction, you will receive a comprehensive eye evaluation before your surgery. This will include a minimum of two refractions (checking your eye glass prescription) at least one week apart, and a careful review of your old prescriptions, when available, to ensure that your prescription is stable. If the prescription is changing or inconsistent you will not be treated. Because pregnancy and nursing can alter the prescription, you cannot take part in this study if you are pregnant or nursing.

To minimize the risk of infection in your eye after surgery, you will use a topical antibiotic



solution until the surface has healed over. During this time, you will be examined every 24 to 48 hours.

To minimize the potential for prolonged surface healing, you will be excluded from participation if you have significantly dry eyes. The amount of epithelium removed during surgery will be kept to a minimum. In addition, artificial tears and bandage contact lenses will be used after the surgery.

To monitor for glaucoma, your intraocular pressure (pressure inside the eye) will be measured while you are taking topical steroid drops. Your post-operative medications will be changed when necessary if your eye pressure is significantly increased.

If you are pregnant, you cannot take part in this study. Women of childbearing age must take a urine pregnancy test before starting this study. If this test is positive, you cannot take part in this study. If you are a woman, you should avoid becoming pregnant for the duration of the study.

15. WHAT ARE THE UNKNOWN RISKS TO YOU OR AN UNBORN CHILD/FETUS

It is not known whether this treatment might harm an unborn child. Therefore, you should not be in this study if you are pregnant. Also, you should not be in this study if you are breast-feeding.

You should avoid becoming pregnant while you are taking part in this study. To avoid becoming pregnant you should either have no sexual relations or use a reliable type of birth control. Except for removal of the uterus (womb) for women and vasectomy (surgical cutting of the tubes that carry sperm) for men, birth control methods are not totally effective in preventing pregnancy. The only ways to completely avoid this risk of the treatment to an unborn baby are (1) avoid pregnancy, or (2) do not take this treatment.

You should avoid becoming pregnant for at least six months after receiving the treatment. Pregnancy within this time after the treatment is done may be a risk to an unborn baby.

16. OTHER PROCEDURES OR TREATMENTS THAT YOU COULD CHOOSE

You may choose to be treated for your nearsightedness without taking part in this study. Should you decide not to participate in this research study, you have the option of continuing to wear either glasses, contact lenses or have these procedures (or other refractive procedure) completed elsewhere. You may also choose to have PRK or LASIK done outside of this study. PRK and LASIK are done at Walter Reed as a standard of care procedures without participation in any research study. Surgical alternatives to PRK and LASIK include laser subepithelial keratectomy (LASEK) and epithelial LASIK (epi-LASIK), radial keratotomy and lens implants. Your doctor can provide you with more information about your nearsightedness, farsightedness and astigmatism and the benefits and risks of the different treatments available. You are encouraged to discuss this with your doctor.



17. IMPORTANT NEW FINDINGS THAT MAY AFFECT YOUR WILLINGNESS TO STAY IN THE STUDY

If we learn new information during the study that could affect your decision to be in this study, we will tell you this information. For example, if we learn about new severe side effects of the treatment, we will tell you about these side effects. The results of the research will be provided to you if you so desire.

18. YOUR RIGHTS IF YOU TAKE PART IN THIS STUDY

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care nor will it affect your military career status.

19. CONTACTS FOR QUESTIONS ABOUT THE STUDY

If you have questions about the study, or if you think you have a study-related injury you should contact the principal investigator at 202-782-6965. For questions about your rights as a research participant, contact the Center Judge Advocate at 202-782-1550, Walter Reed Army Medical Center.

A copy of this consent form will be provided to you.



SIGNATURE OF RESEARCH SUBJECT OR LEGAL REPRESENTATIVE

You have read (or someone has read to you) the information in this consent form. You have been given a chance to ask questions and all of your questions have been answered to your satisfaction.

BY SIGNING THIS CONSENT FORM, YOU FREELY AGREE TO TAKE PART IN THE RESEARCH IT DESCRIBES.

Subject's Signature

Date

Subject's Printed Name

SIGNATURE OF INVESTIGATOR

You have explained the research to the volunteer, or his/her legal representative, and answered all of his/her questions. You believe that the volunteer subject understands the information described in this document and freely consents to participate.

Investigator's Signature

Date (must be the same as the participant's)

Investigator's Printed Name

Version – WRAMC Clinical CF 26 Nov 07.doc



PRK 03 November 2008

**WALTER REED ARMY MEDICAL CENTER
WASHINGTON, D.C**

This Clinical Trial consent form is valid only if it contains the IRB stamped date

Consent for Voluntary Participation in a Clinical Trial (a type of research study) Entitled:

“Optical Quality, Threshold Target Identification, and Military Target Task Performance After Advanced Keratorefractive Surgery – PRK Subprotocol”.

Principal Investigator: COL Kraig S. Bower, MC, Ophthalmology Service, Department of Surgery, phone (202) 782-0202

Study Site: ☐ NNMC, ☐ MPMC, ☒ WRAMC, ☐ USUHS

1. INTRODUCTION OF THE STUDY

You are being asked to be in this research study because you are active duty U.S. Army Soldier and wear either glasses or contact lenses for nearsightedness or astigmatism (unequal curvature of the eyeball). Your participation is voluntary. Refusal will not result in any penalty or loss of benefits to which you are otherwise entitled, nor will refusal have any affect on your military status.

2. PURPOSE OF THE STUDY

The purpose of this research project is to evaluate the outcomes of visual performance in nighttime military settings before and after receiving wavefront guided or wavefront optimized photorefractive keratectomy (PRK) surgery. Although daytime vision is often excellent following refractive surgery, there have been reports of night vision changes resulting from PRK. The information gained will help investigators determine the overall safety and usefulness of the surgery for Army personnel.

Other studies have shown PRK to be safe and effective in the treatment of nearsightedness, farsightedness and astigmatism in civilians and in U.S. Army personnel. In nearsightedness, farsightedness or astigmatism, the clear front surface of your eye, the “cornea”, does not have the proper focusing power. To correct this deficiency you must wear lenses in front of the cornea, either glasses or contacts, in order to see clearly.

PRK uses a machine called an excimer laser to reshape your cornea to try and give it the proper focusing power. To prepare for the laser treatment, the outer layer of cells on the clear part of your eye, the corneal epithelium, is removed exposing the layer to be treated by the laser. Use of the lasers to reshape the cornea is approved by the Food and Drug Administration (FDA) and the procedure is not considered investigational (experimental).

PRK surgeries can be either wavefront guided or wavefront optimized. The wavefront guided



procedure customizes the laser treatments based on the individual characteristics of the eye being corrected. The wavefront optimized procedure uses laser treatment software that has been designed with certain corrections pre-programmed, although a true and customized wavefront plan is not employed.

3. PROCEDURES TO BE FOLLOWED

If you agree to be in this study you will be randomly assigned (similar to the flip of a coin) to one of two groups. Each group will receive one type of refractive surgery, either wavefront guided PRK or wavefront optimized. All treatments will take place at the Center of Refractive Surgery, Walter Reed Army Medical Center.

Demographic data, such as age and gender, will be collected during your screening exam in order to provide a correlation with clinical data. You will undergo eye testing before and at 1, 3, 6 and 12 months after the surgical procedure at Walter Reed Army Medical Center as part of the standard of care (SOC). This will involve measuring vision, refraction (the need for glasses), eye pressure, corneal (the clear transparent outer layer of the eye) curvature, corneal clarity, corneal thickness, and contrast sensitivity (testing your vision under different dark to light contrast conditions). On several examinations these tests will be repeated after your eyes have been dilated with eye drops.

As part of this study, you will be asked to undergo some additional eye testing for research purposes at the eye examination before surgery and at the examinations done 1, 3, 6, and 12 months after surgery. Contrast sensitivity will be measured using a Visual Stimulus Generator, which displays a visual stimulus on a computer monitor and measures time to recognition. A topographic (surface) map of your eye will be obtained using a Wavefront Analyzer. In addition, your vision will be measured using the SuperVision test, which utilizes a chart similar to that used to measure standard visual acuity, though with smaller and more precise lettering. You will also be asked to complete a questionnaire before surgery and 1, 3, 6 and 12 months after surgery to determine your satisfaction with the conventional PRK procedure. It will take you approximately 15 minutes to complete the questionnaire each time it is given. Each clinic appointment will last from one to two hours.

If you are a woman capable of having children, you will be asked to have a urine pregnancy test before the surgical procedure. If this test is positive, you will not be able to continue in this study. All health and personal information collected during the study will be protected. Confidentiality will be maintained by assigning a study ID to the collected information and will not be associated with your name. No information collected will leave Walter Reed Army Medical Center.

4. AMOUNT OF TIME FOR YOU TO COMPLETE THIS STUDY

You will be part of this study for a total of 12 months. During this time, you will be asked to visit the clinic up to 10 times. During the first week after surgery, you will be seen the day after surgery, 3 or 4 days after surgery, and one week after surgery. Each visit will last about 15 to 30



PRK 03 November 2008

minutes. Additional follow-up evaluations will be at 1 month, 3 months, 6 months and 12 months following your surgery. These visits will last up to 1 to 3 hours each. Over the entire twelve months, this will require as much as 10 hours of examination time after the surgery (postoperatively). The standard amount of time for patients not involved in research is eight hours. Research candidates can expect an additional two hours of testing.

5. NUMBER OF PEOPLE THAT WILL TAKE PART IN THIS STUDY

There will be up to 336 people in total taking part in this study. Up to 224 people will be taking part in the PRK portion of the study.

6. POSSIBLE RISKS OR DISCOMFORTS FROM BEING IN THIS STUDY

There are no significant risks that may develop as a result of participation in this study, other than those associated with the procedure itself. None of the testing procedures pose any risk beyond a normal eye examination.

The following are possible risks or discomforts that may develop as a result of undergoing PRK surgery:

- a. Eye discomfort or pain immediately after the procedure. Mild to severe discomfort in the treated eye for several days is common. Eye drops, bandage contact lenses, and oral analgesics are routinely used in the post-operative period to manage pain. In addition, eye patches or other measures may be required during this convalescent period.
- b. Decrease in best-corrected visual acuity (vision with eyeglasses or contact lenses). This complication may occur after up to 7% of treatments. This may improve with treatment. Vision may be treated with glasses post-operatively. Alternatively, contact lenses may be required to improve best-corrected visual acuity. The worst-case would be an inability to correct the visual acuity.
- c. Improper correction. Under-correction (nearsightedness) or over-correction (farsightedness) may occur requiring the use of corrective lenses. There is approximately a 4% chance that you will not achieve 20/40 vision without glasses or contact lenses. You may need to wear glasses or contact lenses after the procedure to attain best vision. Retreatment with another laser procedure may be an option.
- c. Dry eye. Grittiness, scratchiness, foreign body sensation, and fluctuating vision, and sensitivity to dust and smoke are very common in the first 1 to 3 months following surgery. These gradually resolve in the large majority of patients. Up to 5% of patients may have more severe dry eye symptoms that last for a longer period of time. This may require frequent use of lubricant eye drops or other medications to treat the symptoms.
- d. Induced astigmatism. Distortion of vision may require corrective lenses (up to 3%).



- e. Glare and halo from bright lights or halos around lights, especially at night. The glare may be severe enough to cause difficulty driving at night. This usually occurs immediately after the procedure and resolves spontaneously, but may be permanent in approximately 5% of people.
- f. Decrease in contrast sensitivity. This typically occurs immediately after the procedure and usually resolves spontaneously, but may be permanent (up to 3%).
- g. Double vision experienced in one eye. This may occur immediately after the procedure and usually resolves spontaneously as the eye heals. Treatment may be necessary, including corrective lenses or retreatment.
- h. Corneal scarring. Following treatment, your cornea may heal with a scar dense enough to affect the vision (less than 2%). The scar may respond to treatment with medications, but may be permanent and require further surgery, including corneal transplant.
- i. Elevated intraocular pressure. High pressure in the eye may occur while taking eye drops after the procedure (up to 10%). This High pressure usually responds to treatment with topical glaucoma medications.
- j. Recurrent erosions. The corneal epithelium may break down resulting in a painful abrasion. This is treated with topical lubrication and antibiotic medications and may require a therapeutic contact lens (up to 3%).
- k. Microbial keratitis (infection of the cornea) may lead to severe eye damage and loss of vision. Intensive antibiotic therapy is usually required, and surgery may be necessary, including corneal transplant. This complication occurs in less than 0.1% (less than one in one thousand).
- l. Endophthalmitis. A serious and vision threatening infection of the inner tissues of the eye that requires surgery and intensive antibiotics for treatment. Permanent vision loss may result. This complication occurs in less than 0.01% (less than one in ten thousand).
- m. Cataract. Cloudiness of the lens inside the eye, which may reduce vision and require surgery for treatment. (less than 0.1%)

While all risks that we know about have been listed above, other risks about which we do not know may occur or be discovered during future studies. If we find that there was a major risk to you that was not known at the time of your participation in the study, and the risk might have some effect on your health, you will be informed.



7. POSSIBLE BENEFITS FROM BEING IN THIS STUDY

You will not benefit from being in this study, but information we learn may help us gain important knowledge about overall safety and usefulness of the wavefront guided surgery for Army personnel.

8. CONFIDENTIALITY/PRIVACY OF YOUR IDENTITY AND YOUR RESEARCH RECORDS

The principal investigator will keep records of your being in this study. These records may be looked at by people from the Walter Reed Department of Clinical Investigation (DCI), the Walter Reed Human Use Committee (HUC), the Army Clinical Investigation Regulatory Office (CIRO), and other government agencies as part of their duties. These duties include making sure that research subjects are protected. Collaborators of the study will not have access to your medical records. Confidentiality of your records will be protected to the extent possible under existing regulations and laws. Complete confidentiality cannot be promised, particularly for military personnel, because information bearing on your health may be required to be reported to appropriate medical or command authorities. Your name will not appear in any published paper or presentation related to this study.

When you enter this study you will be given a study ID number which will not contain any part of your social security number based on a randomization table. This study ID number, not your name or social security number, will be used to label your study data. The randomization table linking your study ID number with your personal identifying information will be kept in a locked file in the Walter Reed Center for Refractive Surgery, and access to it will be restricted to the principal investigator and his designee(s). All clinical and research data will be kept for 7 years.

This research study meets the confidentiality requirements of the Health Insurance Portability and Accountability Act (HIPAA). A HIPAA authorization form for this study will be provided to you separately, and you will be asked to sign that form.

9. CONDITIONS UNDER WHICH YOUR PARTICIPATION IN THIS STUDY MAY BE STOPPED WITHOUT YOUR CONSENT

Your taking part in this study may be stopped without your consent if remaining in the study might be dangerous or harmful to you. Your taking part in this study may also be stopped without your consent if the military mission requires it, or if you become ineligible for medical care at military hospitals. The principal investigator may terminate your participation in this study if you fail to attend the baseline or follow-up examinations or elect not to undergo the laser procedure.

10. ELIGIBILITY AND PAYMENT FOR BEING IN THIS STUDY

You will not be paid for your participation in this research study.



11. COMPENSATION IF INJURED AND LIMITS TO MEDICAL CARE

Should you be injured as a direct result of being in this study, you will be provided medical care for that injury at no cost to you. You will not receive any compensation (payment) for injury. You should also understand that this is not a waiver or release of your legal rights. You should discuss this issue thoroughly with the principal investigator before you enroll in this study.

Medical care is limited to the care normally allowed for Department of Defense health care beneficiaries (patients eligible for care at military hospitals and clinics). Necessary medical care does not include in-home care or nursing home care.

12. COSTS THAT MAY RESULT FROM TAKING PART IN THIS STUDY

There are no more costs to you for taking part in this study. Indirect costs may be incurred through lost duty time. You will have multiple follow up visits as previously outlined, which may take you away from your duty. The procedure is very safe with a low rate of complications. Most soldiers will be able to return to duty within 24 – 48 hours. If a complication were to develop, the time lost from work would be determined by the complication. Frequently, the complications will be managed on an outpatient basis and no hospitalization expenses are expected.

13. IF YOU DECIDE TO STOP TAKING PART IN THIS STUDY AND INSTRUCTIONS FOR STOPPING EARLY

You have the right to withdraw from this study at any time. If you decide to stop taking part in this study, you should tell the principal investigator as soon as possible. By leaving this study at any time, you in no way risk losing your right to medical care. Some testing or period of observation by the investigators may be recommended for you in order for you to safely stop taking part in this study. Any new significant finding during the course of this study that might affect your willingness to continue participation will be communicated to you.

14. STEPS TAKEN BEFORE AND DURING THIS STUDY TO PROTECT YOU

The surgery will be conducted according to manufacturer's guidelines and in the same way as it would be done if you were not taking part in this study. You will be carefully monitored for complications of the surgery. Any undesired, clinically significant change in the eye or eyes operated on will be evaluated and treated by investigators.

To decrease the likelihood of an incorrect power correction, you will receive a comprehensive eye evaluation before your surgery. This will include a minimum of two refractions (checking your eye glass prescription) at least one week apart, and a careful review of your old prescriptions, when available, to ensure that your prescription is stable. If the prescription is changing or inconsistent you will not be treated. Because pregnancy and nursing can alter the prescription, you cannot take part in this study if you are pregnant or nursing.



PRK 03 November 2008

To minimize the risk of infection in your eye after surgery, you will use a topical antibiotic solution until the surface has healed over. During this time, you will be examined every 24 to 48 hours.

To minimize the potential for prolonged surface healing, you will be excluded from participation if you have significantly dry eyes. The amount of epithelium removed during surgery will be kept to a minimum. In addition, artificial tears and bandage contact lenses will be used after the surgery.

To monitor for glaucoma, your intraocular pressure (pressure inside the eye) will be measured while you are taking topical steroid drops. Your post-operative medications will be changed when necessary if your eye pressure is significantly increased.

If you are pregnant, you cannot take part in this study. Women of childbearing age must take a urine pregnancy test before starting this study. If this test is positive, you cannot take part in this study. If you are a woman, you should avoid becoming pregnant for the duration of the study.

15. WHAT ARE THE UNKNOWN RISKS TO YOU OR AN UNBORN CHILD/FETUS

It is not known whether this treatment might harm an unborn child. Therefore, you should not be in this study if you are pregnant. Also, you should not be in this study if you are breast-feeding.

You should avoid becoming pregnant while you are taking part in this study. To avoid becoming pregnant you should either have no sexual relations or use a reliable type of birth control. Except for removal of the uterus (womb) for women and vasectomy (surgical cutting of the tubes that carry sperm) for men, birth control methods are not totally effective in preventing pregnancy. The only ways to completely avoid this risk of the treatment to an unborn baby are (1) avoid pregnancy, or (2) do not take this treatment.

You should avoid becoming pregnant for at least six months after receiving the treatment. Pregnancy within this time after the treatment is done may be a risk to an unborn baby.

16. OTHER PROCEDURES OR TREATMENTS THAT YOU COULD CHOOSE

You may choose to be treated for your nearsightedness without taking part in this study. Should you decide not to participate in this research study, you have the option of continuing to wear either glasses, contact lenses or have these procedures (or other refractive procedure) completed elsewhere. You may also choose to have PRK or LASIK done outside of this study. PRK and LASIK are done at Walter Reed as a standard of care procedures without participation in any research study. Surgical alternatives to PRK and LASIK include laser subepithelial keratectomy (LASEK) and epithelial LASIK (epi-LASIK), radial keratotomy and lens implants. Your doctor can provide you with more information about your nearsightedness, farsightedness and astigmatism and the benefits and risks of the different treatments available. You are encouraged to discuss this with your doctor.



17. IMPORTANT NEW FINDINGS THAT MAY AFFECT YOUR WILLINGNESS TO STAY IN THE STUDY

If we learn new information during the study that could affect your decision to be in this study, we will tell you this information. For example, if we learn about new severe side effects of the treatment, we will tell you about these side effects. The results of the research will be provided to you if you so desire.

18. YOUR RIGHTS IF YOU TAKE PART IN THIS STUDY

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care nor will it affect your military career status.

19. CONTACTS FOR QUESTIONS ABOUT THE STUDY

If you have questions about the study, or if you think you have a study-related injury you should contact the principal investigator at 202-782-6965. For questions about your rights as a research participant, contact the Center Judge Advocate at 202-782-1550, Walter Reed Army Medical Center.

A copy of this consent form will be provided to you.



PRK 03 November 2008

SIGNATURE OF RESEARCH SUBJECT OR LEGAL REPRESENTATIVE

You have read (or someone has read to you) the information in this consent form. You have been given a chance to ask questions and all of your questions have been answered to your satisfaction.

BY SIGNING THIS CONSENT FORM, YOU FREELY AGREE TO TAKE PART IN THE RESEARCH IT DESCRIBES.

Subject's Signature

Date

Subject's Printed Name

SIGNATURE OF INVESTIGATOR

You have explained the research to the volunteer, or his/her legal representative, and answered all of his/her questions. You believe that the volunteer subject understands the information described in this document and freely consents to participate.

Investigator's Signature

Date (must be the same as the participant's)

Investigator's Printed Name

Version – WRAMC Clinical CF 26 Nov 07.doc

Approved by the WRAMC HUC/IRB on 03 November 2008 (Per CIRO) for WU # 08-6967.
This form expires on 12 August 2009 Initials MG.



**Authorization for Research Use of Protected Health Information
Walter Reed Army Medical Center (WRAMC)**

Protocol Title: Optical Quality, Threshold Target Identification, and Military Target Task Performance After Advanced Keratorefractive Surgery

Principal Investigator: COL Kraig S. Bower, MC

Work Unit #: 08-6067

The Federal Health Insurance Portability and Accountability Act (HIPAA) includes a Privacy Rule that gives special safeguards to Protected Health Information (PHI) that is identifiable, in other words, can be directly linked to you (for example, by your name, Social Security Number, birth date, etc.). We are required to advise you how your PHI will be used.

1. What information will be collected?

For this research study, we will be collecting information about your eye examinations, refractive surgery, eye health status, any side effects that you are experiencing, and how the treatment affects your comfort. These include vision, refraction (the need for glasses), eye pressure, corneal (the clear transparent outer layer of the eye) curvature, corneal clarity, corneal thickness, wavefront analysis and contrast sensitivity (testing your vision under different dark to light contrast conditions). Some patients will have additional testing in night vision performance that will be also be collected. We will also be collecting your (PHI) such as your name, age, telephone and fax numbers, email address and your social security number.

2. Who may use my PHI within the Military Healthcare System?

The members of the Center for Refractive Surgery research team will have access to your health information in order to find out if you qualify to participate in this study, to plan and conduct your surgery, to administer research medication, to monitor your progress, and to analyze the research data. Additionally, your PHI may be made available to health oversight groups such as the WRAMC Department of Clinical Investigation and the WRAMC Institutional Review Board.

3. What persons outside of the Military Healthcare System who are under the HIPAA requirements will receive my PHI?

No persons outside the Military Healthcare System will be sent your PHI.

4. What is the purpose for using or disclosing my Protected Health Information (PHI)?

Your protected health information will be collected and used during the course of the research study, to monitor your health status, to measure the effects of drugs or devices or procedures, to determine research results, and to possibly develop new tests and procedures.

The information may also be reviewed when the research study is audited for compliance. When the study is over, you have the right to see the information and copy it for your records.



A PHOTOCOPY OF THIS FORM MUST BE SIGNED BY ALL VOLUNTEERS.

Approved by the WRAMC Privacy Officer on 10/15/08 for WU# 08-6067 Expires 12 Aug 2013

Z. Harper

**Authorization for Research Use of Protected Health Information
Walter Reed Army Medical Center (WRAMC)**

5. How long will the researchers keep my Protected Health Information?

The WRAMC research team in the Center for Refractive Surgery will keep the research data and all other identification documents for up to seven years after the end of the study. At the end of this time the data will be destroyed.

6. Can I review my own research information?

Because the research includes blinding research participants to their study group, you will not be able to look at your research information until your participation in the study has ended.

7. Can I cancel this Authorization?

Yes. If you cancel this Authorization, you will no longer be included in the research study. However, the information that has already been collected will be kept by the research team to assure patient safety. If you want to cancel your Authorization, please contact the Principal Investigator in writing.

If you decide to participate in this research study, your Authorization for this study will not expire unless you revoke or cancel it in writing to the research doctor. If you revoke your Authorization, you will also be removed from the study, but standard medical care and any other benefit to which you are entitled will not be affected in any way.

8. What will happen if I decide not to sign this Authorization?

If you decide not to sign this Authorization, you will not be able to participate in this research study. Refusal to sign this Authorization will not result in any loss of medical benefits to which you are otherwise entitled.

9. Can my Protected Health Information be disclosed to parties not included in this Authorization who are not under the HIPAA requirements?

There is a potential that your research information will be shared with another party not listed in this Authorization in order to meet legal or regulatory requirements. Examples of persons who may access your PHI include representatives of the Clinical Investigation Regulatory Office, the Food and Drug Administration, the Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP), and the DHHS Office for Civil Rights. This disclosure is unlikely to occur, but in that case, your health information would no longer be protected by the HIPAA Privacy Rule.

10. Who should I contact if I have any complaints?

If you believe your privacy rights have been violated, you may file a written complaint with the WRAMC Privacy Officer, located at 6900 Georgia Ave., NW, Washington, DC 20307. Telephone: 202-782-3501.



A PHOTOCOPY OF THIS FORM MUST BE SIGNED BY ALL VOLUNTEERS.

Approved by the WRAMC Privacy Officer on 10/15/08 for WU# 08-6067 Expires 12 Aug 2013

[Signature]

**Authorization for Research Use of Protected Health Information
Walter Reed Army Medical Center (WRAMC)**

By signing this document I authorize WRAMC personnel to use and disclose my Protected Health Information (PHI) collected about me for research purposes as described above. My signature below acknowledges receipt of a copy of this Authorization:

Signature: _____ Date: _____

If you are a parent, court-appointed representative, or acting as power of attorney, indicate your authority to act for the participant: _____

Print Name: _____

A copy of this signed Authorization will be provided to you.

Version -WRAMC HIPAA Authorization 23March07.doc



A PHOTOCOPY OF THIS FORM MUST BE SIGNED BY ALL VOLUNTEERS.

Approved by the WRAMC Privacy Officer on 10/8/08 for WU# 08-6067 Expires 12 Aug 2013

Z. Harper